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[From this paper onwards, the questions will be not released officially; so these would be the recall questions which implies that the fine grammar & wordings being exchanged due to recall bias is known]

Paper 1

1.a. Pulmonary function test done by spirometer

- Spirometry is a non-invasive, relatively simple, and highly valuable test in the diagnosis and management of respiratory diseases
- It is crucial for the assessment of symptoms like shortness of breath, chronic cough, and wheezing
- The interpretation of spirometry results should be done in the context of the patient's clinical history, physical examination, and other diagnostic findings
- Regular spirometry testing is also important for monitoring lung diseases over time, especially for conditions like asthma, where management may involve adjusting medications based on lung function.

Parameters Measured in Pediatric Spirometry

FVC (Forced Vital Capacity); FEV1 (Forced Expiratory Volume in 1 second); FEV1/FVC Ratio; PEF (Peak Expiratory Flow)

Test Component	Description	Clinical Significance
Forced Vital Capacity (FVC)	Total amount of air exhaled forcefully after a deep inhalation.	Reduced in restrictive lung diseases.
Forced Expiratory Volume in 1 Second (FEV1)	Amount of air exhaled in the first second of a forced exhalation.	Reduced in obstructive lung diseases.
FEV1/FVC Ratio	Compares FEV1 to FVC as a percentage.	A reduced ratio (<70%) indicates obstructive lung disease; normal/high suggests restrictive lung disease.
Peak Expiratory Flow (PEF)	Highest flow rate achieved during the maximal expiration.	Useful for asthma monitoring; reduced in obstructive lung diseases.
Forced Expiratory Flow 25-75% (FEF25-75%)	Average flow rate during the middle half of the FVC maneuver.	Reduced in small airway diseases.
Total Lung Capacity (TLC)	Total volume of air in the lungs after maximum inhalation.	Increased in obstructive lung diseases; decreased in restrictive diseases.
Residual Volume (RV)	Volume of air remaining in the lungs after a maximal exhalation.	Increased in obstructive lung diseases.

Vital Capacity (VC)	Total volume of air that can be exhaled after a full inhalation.	Reduced in both obstructive and restrictive lung diseases.
Spirometry Pre- and Post-Bronchodilator Tests	Assess reversibility of airway obstruction by comparing results before and after bronchodilator use.	Improvement post-bronchodilator suggests reversible obstructive lung disease (e.g., asthma).
Flow-Volume Loops	Graphical representation of the rate of flow against the volume of air inhaled or exhaled.	Helps identify patterns associated with different types of lung diseases.

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1.b. Explain pulmonary function test with diagrammatic representation.

Understanding the clinical utility of PFTs allows for a more nuanced approach to pediatric respiratory care, from diagnosis to treatment and beyond.

- ❖ Pulmonary Function Tests (PFTs) are a suite of diagnostic procedures that evaluate the functional status of the lungs.
- ❖ They are instrumental in diagnosing, monitoring, and managing respiratory diseases, particularly in the pediatric population.

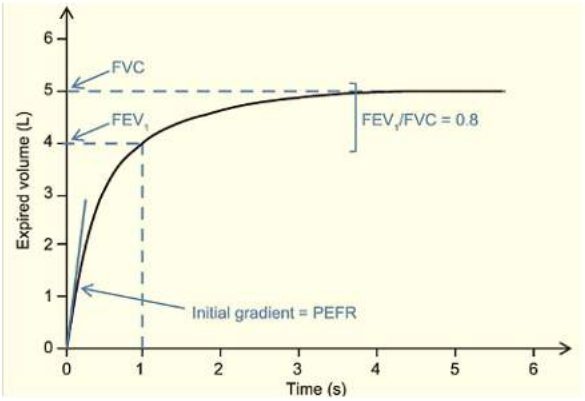
Types of Pulmonary Function Tests

1. Spirometry
2. Lung Volumes and Capacities
3. Diffusion Capacity
4. Airway Resistance Tests
5. Bronchial Provocation Tests

Important PFT Parameters:

1. Forced Vital Capacity (FVC)

- **Definition**: The total volume of air that can be forcibly exhaled after a maximal inhalation.
- **Clinical Significance**:
  - Evaluates lung capacity and restrictive lung diseases.



- A reduced FVC suggests restrictive pathology like interstitial lung disease or chest wall deformities.
- Lower values in younger children due to smaller lung size.
- Influenced by height, age, and gender.

- **Interpretation**:
  - Values are compared to predicted norms.
  - Values <80% of the predicted are generally considered abnormal.

2. Forced Expiratory Volume in 1 second (FEV1)

- **Definition**: The volume of air that can be forcibly exhaled in the first second during an FVC maneuver.
- **Clinical Significance**:
  - Most commonly used parameter for diagnosing obstructive diseases like asthma and cystic fibrosis.
  - Lower in younger children due to smaller airway diameter.
  - Also influenced by height and age.
- **Interpretation**:
  - Values <80% of the predicted suggest obstructive pathology.
  - Used in combination with FVC to calculate FEV1/FVC ratio.

3. FEV1/FVC Ratio

- **Definition**: The ratio of FEV1 to FVC, expressed as a percentage.
- **Clinical Significance**:
  - Distinguishes between obstructive and restrictive lung diseases.
  - A reduced ratio (<70%) indicates obstructive disease.
  - Children with asthma may show variability in this ratio.
  - Useful for monitoring disease progression and treatment efficacy.
- **Interpretation**:
  - Values are age-specific.
  - Values <70% are indicative of obstructive diseases.

4. Peak Expiratory Flow (PEF)

- **Definition**: The maximum flow rate generated during a forceful exhalation, starting from full lung inflation.
- **Clinical Significance**:
  - Useful for assessing the severity of airway obstruction.
  - Often used in the management and diagnosis of asthma.
  - Portable PEF meters are available for home monitoring.
  - Useful for assessing acute asthma exacerbations.
- **Interpretation**:
  - Compared against predicted or personal best values.
  - Significant drops indicate acute exacerbation in conditions like asthma.

Reference Values

- Age, height, gender, and ethnic background are considered for normative data.

Interpretative Strategies

1. **Obstructive Patterns**
   - Reduced FEV1/FVC ratio
   - Reduced PEF
2. **Restrictive Patterns**
   - Reduced FVC
   - Normal or increased FEV1/FVC ratio
3. **Mixed Patterns**
   - Reduced FVC, FEV1, and FEV1/FVC ratio

Clinical Utility of Pulmonary Function Tests

1. Diagnostic Utility

- **Identification of Disease Type**: Distinguishes between obstructive and restrictive lung diseases.
- **Early Detection**: Useful in identifying diseases like asthma and cystic fibrosis in their early stages.

2. Monitoring and Prognosis

- **Treatment Efficacy**: Evaluates the effectiveness of therapeutic interventions.
- **Disease Progression**: Monitors the course of chronic diseases over time.

3. Preoperative Assessment

- **Risk Stratification**: Assesses the risk of pulmonary complications in surgeries.

4. Occupational Health

- **Exposure Assessment**: Evaluates lung function in children exposed to occupational hazards like dust or chemicals.

5. Research and Clinical Trials

- **Outcome Measures**: Serves as a reliable outcome measure in research studies.

Specific Clinical Scenarios in Pediatrics

1. **Asthma**
    - Spirometry for diagnosis and management.
    - Bronchial Provocation Tests for assessing airway hyper-responsiveness.
2. **Cystic Fibrosis**
    - Spirometry and lung volumes for monitoring disease progression.
    - Diffusion capacity for assessing alveolar function.
3. **Interstitial Lung Disease**
    - Lung volumes and diffusion capacity for diagnosis and monitoring.
4. **Preoperative Assessment**
    - Spirometry and lung volumes for risk assessment in surgeries like scoliosis correction.
5. **Bronchiolitis**
    - Airway resistance tests for assessing disease severity.

Pediatric Drug Dosages for PFT-Induced Bronchoconstriction

- **Albuterol**: 0.1-0.2 mg/kg
- **Ipratropium Bromide**: 250-500 mcg for children >12 years

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2.a. Infant mortality rate and it's causes

- The infant mortality rate is defined as the number of deaths of children under one year of age, expressed per 1000 live births
- The current infant mortality rate (IMR) for India in 2023 is 26.619 deaths per 1,000 live births

- This represents a 3.89% decline from the previous year, 2022, when the IMR was 27.695 deaths per 1,000 live births
- The decline in IMR is a positive indicator of improvements in healthcare, socio-economic conditions, and public health initiatives in India.

- Efforts to reduce infant mortality in India focus on improving maternal health, enhancing healthcare infrastructure, increasing vaccination coverage, and addressing socio-economic determinants of health.

Causes: Broadly can be classified into neonatal causes and others.

- Neonatal deaths contribute to ~54.3% of infant deaths and 39% occurred on the first day of life.
- Birth asphyxia followed by low birth weight (LBW)/prematurity are the most common causes of neonatal death, while infection is the most common cause of post-neonatal death.

1. **Preterm Birth Complications:** Babies born before 37 weeks of gestation are at a higher risk of health complications and mortality due to underdeveloped organs.
2. **Neonatal Infections:** Infections like sepsis, pneumonia, and meningitis are significant causes of neonatal deaths.
3. **Birth Asphyxia and Birth Trauma:** Lack of oxygen during birth or physical injuries sustained during the birthing process can be fatal.
4. **Acute Respiratory Infections:** Pneumonia and other respiratory infections are leading causes of infant mortality, particularly in areas with poor air quality.
5. **Diarrheal Diseases:** Poor sanitation and lack of clean water contribute to diarrheal diseases, which can be deadly for infants.
6. **Congenital Anomalies:** Birth defects such as congenital heart defects, neural tube defects, and gastrointestinal malformations are significant contributors to infant mortality.
7. **Malnutrition:** Undernutrition and malnutrition, including both macronutrient and micronutrient deficiencies, play a critical role in infant mortality.
8. **Low Birth Weight:** Infants with low birth weight, often due to maternal malnutrition or premature birth, have a higher risk of mortality.
9. **Immunizable Diseases:** Despite vaccination efforts, diseases like **measles**, tetanus, and tuberculosis still contribute to infant mortality.

10. **Maternal Health Factors:** Maternal health issues, including complications during pregnancy and childbirth, can directly impact infant survival.

GOI - Interventions for improving Infant Mortality Rate (IMR)

These interventions represent a comprehensive approach by the Indian government to address various factors contributing to infant mortality, ranging from healthcare infrastructure improvements to community-based initiatives and public health campaigns.

1. **Facility Based New-born Care:**
    - Establishes Sick New-born Care Units (SNCUs) at hospitals and New-born Stabilization Units (NBSUs) at health centers to provide specialized care for sick and small babies.
2. **Community Based Care of New-born and Young Children:**
    - Involves ASHAs conducting home visits under the Home Based New-born Care (HBNC) and Home-Based Care of Young Children (HBYC) programs, focusing on child rearing practices and early identification of sick new-borns and young children.
3. **Mothers' Absolute Affection (MAA):**
    - Promotes early breastfeeding initiation, exclusive breastfeeding for the first six months, and appropriate Infant and Young Child Feeding (IYCF) practices.
4. **Social Awareness and Actions to Neutralize Pneumonia Successfully (SAANS):**
    - Launched in 2019, this initiative aims to reduce childhood morbidity and mortality due to pneumonia.
5. **Universal Immunization Programme (UIP):**
    - Provides vaccinations against critical diseases like Tuberculosis, Diphtheria, Pertussis, and others, including the introduction of Rotavirus and Pneumococcal Conjugate Vaccines.
6. **Rashtriya Bal Swasthya Karyakaram (RBSK):**
    - Screens children up to 18 years for 30 health conditions and provides intervention through District Early Intervention Centres (DEICs).
7. **Nutrition Rehabilitation Centres (NRCs):**

- Established at public health facilities to treat children with Severe Acute Malnutrition (SAM) with medical complications.

8. **Intensified Diarrhoea Control Fortnight / Defeat Diarrhoea (D2):**
    - Focuses on promoting ORS and Zinc use to reduce diarrhoeal deaths.
9. **Anaemia Mukt Bharat (AMB):**
    - A strategy under POSHAN Abhiyan to combat anaemia through testing, treatment, addressing non-nutritional causes, and comprehensive communication.
10. **Capacity Building:**
    - Involves training healthcare providers to improve maternal and child health outcomes.

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2.b. Sustainable development goals

- The Sustainable Development Goals (SDGs) are a collection of 17 interlinked global goals designed to be a "blueprint to achieve a better and more sustainable future for all.
- " Set in 2015 by the United Nations General Assembly and intended to be achieved by the year 2030, these goals are part of the UN's 2030 Agenda for Sustainable Development
- Each goal has specific targets to be achieved, and the SDGs are universal, calling for action by all countries—developed, developing, and underdeveloped—to promote prosperity while protecting our planet.
- They recognize that ending poverty and other deprivations must go hand-in-hand with strategies that improve health and education, reduce inequality, and spur economic growth – all while tackling climate change and working to preserve our oceans and forests.

Goals:

1. **No Poverty:** End poverty in all its forms everywhere.
2. **Zero Hunger:** End hunger, achieve food security and improved nutrition, and promote sustainable agriculture.
3. **Good Health and Well-being:** Ensure healthy lives and promote well-being for all at all ages.

4. **Quality Education:** Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all.
5. **Gender Equality:** Achieve gender equality and empower all women and girls.
6. **Clean Water and Sanitation:** Ensure availability and sustainable management of water and sanitation for all.
7. **Affordable and Clean Energy:** Ensure access to affordable, reliable, sustainable, and modern energy for all.
8. **Decent Work and Economic Growth:** Promote sustained, inclusive, and sustainable economic growth, full and productive employment, and decent work for all.
9. **Industry, Innovation, and Infrastructure:** Build resilient infrastructure, promote inclusive and sustainable industrialization, and foster innovation.
10. **Reduced Inequalities:** Reduce inequality within and among countries.
11. **Sustainable Cities and Communities:** Make cities and human settlements inclusive, safe, resilient, and sustainable.
12. **Responsible Consumption and Production:** Ensure sustainable consumption and production patterns.
13. **Climate Action:** Take urgent action to combat climate change and its impacts.
14. **Life Below Water:** Conserve and sustainably use the oceans, seas, and marine resources for sustainable development.
15. **Life on Land:** Protect, restore, and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss.
16. **Peace, Justice, and Strong Institutions:** Promote peaceful and inclusive societies for sustainable development, provide access to justice for all, and build effective, accountable, and inclusive institutions at all levels.
17. **Partnerships for the Goals:** Strengthen the means of implementation and revitalize the global partnership for sustainable development.

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3.a. Risk factors for injury in children

The risk factors for injury in children are many and can be influenced by a lot of environmental, social, and individual factors.

1. **Age and Developmental Stage:**
    - Younger children are at higher risk for certain types of injuries (e.g., drowning, burns) due to their limited physical coordination and cognitive abilities.

- Adolescents may engage in riskier behaviors, increasing their susceptibility to injuries from activities like driving or sports.

2. **Gender:**
   - Boys are generally at a higher risk for injuries than girls, possibly due to differences in risk-taking behaviors and activities.
3. **Socioeconomic Status:**
   - Lower socioeconomic status is associated with a higher risk of injuries, often due to environmental factors like unsafe housing and limited access to safety equipment.
4. **Environmental Factors:**
   - Unsafe play areas, lack of safe pedestrian routes, and exposure to hazardous materials increase the risk of injuries.
   - Poorly designed or maintained public spaces and playgrounds can lead to accidents.
5. **Lack of Supervision:**
   - Inadequate adult supervision, especially for younger children, significantly increases the risk of injuries.
6. **Unsafe Home Environment:**
   - Hazards such as open water sources, unsecured furniture, accessible toxic substances, and lack of safety devices (smoke alarms, window guards) contribute to injury risk. Below are necessary strategies to tackle:

Home Safety Aspect	Strategy	Details/Examples
Childproofing	Secure potentially dangerous areas	Lock cabinets containing chemicals or sharp objects Install safety gates at staircases Use window guards
Safe Sleeping Practices	Ensure a safe sleeping environment	Use appropriate cribs Avoid soft bedding and pillows to prevent suffocation
Water Safety	Prevent accidents in bathrooms and kitchens	Supervise bath time Set water heater temperatures to prevent scalds Install anti-scald devices on faucets
Poison Prevention	Store hazardous substances safely	Keep medicines, cleaning agents, and toxic substances out of children's reach Use child-resistant packaging
Fire Safety	Prepare for and prevent fire-related accidents	Install smoke detectors in key areas Keep fire extinguishers accessible Plan and practice fire escape routes

Electrical Safety	Prevent electrical accidents	Cover electrical outlets Keep electrical cords out of reach Ensure electrical appliances are in good condition
Furniture and Appliance Safety	Secure heavy objects and furniture	Anchor heavy furniture to walls Keep heavy objects on lower shelves Secure TVs and other heavy appliances
Kitchen Safety	Make the kitchen a safe area	Keep knives and sharp tools in locked drawers Turn pot handles inward on the stove Supervise children in the kitchen
Window and Balcony Safety	Prevent falls from heights	Install window guards or locks Ensure balcony railings are secure and high enough
Pet Safety	Safe interactions with household pets	Supervise interactions between children and pets Educate children on how to safely approach and handle pets

7. **Behavioral and Psychological Factors:**
    - Children those with hyperactivity, impulsivity, or certain behavioral disorders may be more prone to injuries.
    - Peer pressure and the desire to fit in can lead adolescents to engage in injury prone risky behaviors.
8. **Lack of Safety Equipment:**
    - Not using appropriate safety gear like helmets, seat belts, and life jackets increases the risk of severe injury in accidents.
9. **Exposure to Violence:**
    - Children exposed to violence, whether in the community or at home, are at a higher risk of both physical and psychological injuries.
10. **Cultural and Social Norms:**
    - Some Practices and norms that do not prioritize child safety, such as resistance to using child safety seats, can increase injury risk.
11. **Limited Knowledge of Safety Practices:**
    - Parents' or caregivers' lack of awareness about child safety measures can inadvertently put children at risk.
12. **Physical and Mental Health Conditions:**
    - Children with certain health conditions (e.g., epilepsy, vision or hearing impairments) may have an increased risk of injuries.
13. **Substance Abuse:**
    - In older children and adolescents, substance abuse (alcohol, drugs) is a significant risk factor for injuries.

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3.b. Bullying and cyberbullying

Bullying and cyberbullying are significant issues affecting children and adolescents worldwide today, with serious implications for their mental and physical well-being.

Bullying:

1. **Definition:**
   - Bullying is intentional, aggressive behavior that involves an imbalance of power or strength. It can be physical, verbal, or social.
2. **Forms:**
   - Physical (hitting, pushing)
   - Verbal (teasing, threats)
   - Social or Relational (spreading rumors, exclusion)
3. **Environment:**
   - Typically occurs in physical settings like schools, playgrounds, and communities.
4. **Detection:**
   - Often more observable by peers, teachers, and parents.
5. **Impact:**
   - Leads to psychological distress, anxiety, depression, and in severe cases, self-harm or suicidal ideation.
   - Affects academic performance and social relationships.

Cyberbullying:

1. **Definition:**
   - Cyberbullying involves bullying using digital means, such as social media, text messages, emails, and websites.
2. **Forms:**
   - Sending threatening emails or messages
   - Spreading rumors or posting hurtful content online
   - Impersonating someone and sending damaging messages (An app called DEEPFAKE is used for this; Laws don't exist yet on it!)
3. **Environment:**
   - Occurs in the digital realm, making it pervasive with a potentially larger audience.
4. **Detection:**
   - More challenging to detect as it can occur at any time and often anonymously.
5. **Impact:**

- Can lead to severe emotional distress, feeling of isolation, and difficulty escaping the harassment.
- May have a broader audience, leading to intensified shame or embarrassment.

Commonalities and Differences:

- **Commonalities:**
  - Both can lead to significant emotional and psychological harm.
  - Involve power imbalances and repeated aggression.
  - Can co-occur; victims of one type are often victims of the other.
- **Differences:**
  - Cyberbullying can occur 24/7 and reach a victim anywhere, making it more pervasive.
  - Anonymity is more common in cyberbullying, complicating efforts to address the behavior.
  - Cyberbullying leaves a digital footprint, which can be used as evidence.

Addressing Bullying and Cyberbullying:

- **Prevention and Education:**
  - Schools and communities should implement comprehensive bullying prevention programs.
  - Educating children and adolescents about responsible online behavior and the consequences of cyberbullying.
- **Support and Intervention:**
  - Providing support to victims, including counseling and mental health services.
  - Encouraging bystanders to speak up and report bullying incidents.
- **Policy and Legislation:**
  - Implementing and enforcing anti-bullying policies and laws.
  - Schools and online platforms should have clear protocols for dealing with bullying and cyberbullying.
- **Parental and Guardian Involvement:**
  - Parents should be aware of their children's online activities and foster open communication.
  - Encouraging children to report any bullying incidents.

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4.a. Robust quality criteria

- In medical research, robust quality criteria are essential to ensure the reliability, validity, and generalizability of study findings. These criteria are critical in evaluating the strength of evidence and in guiding clinical decision-making.
- Robust quality criteria in medical research are pivotal in ensuring that the findings are credible, ethically sound, and applicable to patient care. Adherence to these criteria strengthens the evidence base that informs clinical practice and healthcare policy.

1. Study Design

- **Randomization**: Reduces bias by equally distributing known and unknown factors among groups in clinical trials.
- **Control Group**: Essential for comparing the intervention's effect.
- **Blinding**: Minimizes bias by preventing the knowledge of treatment allocation from influencing the outcome assessment or treatment.

2. Sample Size and Power

- **Adequate Sample Size**: Ensures sufficient power to detect a clinically significant effect.
- **Power Analysis**: Conducted to determine the minimum sample size needed based on expected effect size and variance.

3. Data Quality and Management

- **Data Accuracy and Consistency**: Rigorous data collection and entry processes.
- **Data Monitoring**: Regular checks for data integrity and completeness.

4. Ethical Considerations

- **Informed Consent**: Ensuring participants are fully informed about the study's risks and benefits.
- **Ethical Approval**: Obtained from relevant institutional review boards or ethics committees.

5. Outcome Measures

- **Valid and Reliable Measures**: Use of standardized, validated tools for outcome assessment.

- **Primary and Secondary Outcomes**: Clearly defined and relevant to the study objectives.

6. Statistical Analysis

- **Appropriate Statistical Methods**: Matching the analysis techniques to the study design and data type.
- **Handling of Missing Data**: Addressing missing data appropriately to avoid bias.
- **Adjustment for Confounders**: Using statistical methods to control for potential confounding variables.

7. Reporting Standards

- **Transparent Reporting**: Following guidelines like CONSORT for trials or STROBE for observational studies.
- **Disclosure of Conflicts of Interest**: Transparency about potential biases due to financial or other interests.

8. External Validity

- **Generalizability**: Assessing whether the study findings are applicable to a broader population.
- **Real-world Relevance**: Ensuring the study context and population reflect real clinical scenarios.

9. Replicability

- **Reproducibility of Results**: Ability of other researchers to replicate findings under similar conditions.

10. Peer Review and Publication

- **Critical Review**: Undergoing rigorous peer review before publication.
- **Publication in Reputable Journals**: Ensures a wider and more critical audience.

Quality Criteria	Description and Importance
Study Design	Incorporates randomization, control groups, and blinding to reduce bias and enhance reliability.
Sample Size and Power	Ensures sufficient sample size for statistical power to detect significant effects. Involves power analysis.

Data Quality and Management	Focuses on accuracy, consistency, and regular monitoring of data.
Ethical Considerations	Includes informed consent and ethical approval to uphold research integrity and participant safety.
Outcome Measures	Utilizes valid and reliable tools for assessing primary and secondary outcomes.
Statistical Analysis	Employs appropriate methods, addresses missing data, and adjusts for confounders to ensure accurate results.
Reporting Standards	Adheres to guidelines like CONSORT or STROBE for transparent reporting and disclosure of conflicts of interest.
External Validity	Assesses the generalizability and real-world relevance of the study findings.
Replicability	Ensures that the study results can be replicated under similar conditions by other researchers.
Peer Review and Publication	Involves critical review and publication in reputable journals for wider scrutiny and acceptance.

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4.b. PRISM score

- The PRISM score, - Pediatric Risk of Mortality score, is widely used clinical assessment tool designed to evaluate the severity of illness and predict mortality risk in pediatric intensive care units (PICUs).
- It is based on physiological and laboratory data collected during the first 24 hours of a child's admission to the PICU.
- The PRISM score is part of a broader category of scoring systems used in critical care medicine to assess the severity of illness and guide clinical decision-making.

1. **Purpose:**
   - To quantify the severity of illness in critically ill pediatric patients.
   - To predict the risk of mortality based on the patient's condition upon PICU admission.
2. **Parameters Measured:**
   - The PRISM score includes various physiological and laboratory parameters, such as heart rate, blood pressure, temperature, pH level, and blood gas analysis.
   - These parameters reflect the functioning of different organ systems (cardiovascular, respiratory, renal, hepatic, hematologic, and neurologic).

3. **Scoring System:**
    - Each parameter is assigned a score based on how far it deviates from the normal range.
    - The total score is calculated by summing the scores of all individual parameters.
    - A higher PRISM score indicates a more severe illness and a higher risk of mortality.
4. **Versions:**
    - The original PRISM score was developed in the 1980s and has undergone several revisions to improve its accuracy and applicability, leading to the development of PRISM III and PRISM IV.
5. **Clinical Application:**
    - Used by healthcare professionals to assess the severity of illness in pediatric patients admitted to the PICU.
    - Helps in resource allocation, decision-making regarding the level of care, and informing discussions with families about prognosis.
6. **Limitations:**
    - The score is based on data from the first 24 hours of PICU admission, which may not capture subsequent clinical changes.
    - It requires accurate and comprehensive data collection, which can be resource-intensive.
    - While useful for population-level predictions, its accuracy for individual patient prognosis can vary.
7. **Comparison with Other Scores:**
    - The PRISM score is one of several scoring systems used in PICUs, others include the Pediatric Index of Mortality (PIM) and the Sequential Organ Failure Assessment (SOFA) score.
    - Each scoring system has its own strengths and limitations, and the choice of which to use may depend on the specific clinical setting and available resources.
8. **Research and Quality Improvement:**
    - PRISM scores are often used in research studies to characterize patient populations and outcomes.
    - They can also be used in quality improvement initiatives to benchmark and improve PICU performance.

PRISM III score components,
which include physiological and laboratory variables:

(The points for each variable range from 0 to 4, with higher points indicating greater severity. The total PRISM III score is the sum of all the points, which can then be used to calculate the predicted mortality risk.)

Variable	Points
Physiological Variables	
Temperature (°C)	0-4
Mean Arterial Pressure (mmHg)	0-4
Heart Rate (beats/min)	0-4
Respiratory Rate (breaths/min)	0-4
Pupillary Reaction	0/3
Laboratory Variables	
PaO2/FiO2 ratio	0-4
PaO2 (mmHg)	0-4
PaCO2 (mmHg)	0-4
pH	0-4
HCO3- (mEq/L)	0-4
Sodium (mEq/L)	0-4
Potassium (mEq/L)	0-4
Calcium (mg/dL)	0-4
Glucose (mg/dL)	0-4
Blood Urea Nitrogen (mg/dL)	0-4
Creatinine (mg/dL)	0-4
Total Bilirubin (mg/dL)	0-4
Albumin (g/dL)	0-4
White Blood Cell Count	0-4
Additional Variables	
Mechanical Ventilation	0/4

Pupillary Reaction	0/3

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5.a. Religious and cultural objections in health care

- Religious and cultural objections in healthcare are diverse and complex, reflecting the our country's rich tapestry of beliefs, traditions, and practices.
- India's population includes a wide array of religions, including Hinduism, Islam, Christianity, Sikhism, Buddhism, and Jainism, among others.
- Each of these religions, along with various cultural practices, can influence perceptions and decisions regarding health care.
- Understanding these objections is crucial for healthcare providers to offer culturally sensitive and respectful care and at the same time safeguard the patients from its untoward effects.

1. **Hinduism:**
   - **Dietary Restrictions:** Many Hindus are vegetarian and may refuse medications derived from animals.
   - **End-of-Life Care:** Preferences for dying at home, reluctance towards aggressive life-support measures, and specific rituals after death.
   - **Fasting Practices:** Observance of fasts might affect medication schedules and nutritional interventions.
2. **Islam:**
   - **Modesty Concerns:** Preference for same-gender healthcare providers, especially for women.
   - **Dietary Laws:** Halal dietary restrictions may affect medication acceptability and nutritional support.
   - **Refusal of porcine based surfactants:** In neonates with RDS
   - **Refusal of donor human milk**
   - **Fasting During Ramadan:** Impacts medication schedules and management of chronic conditions like diabetes.
3. **Christianity:**
   - **Variability in Beliefs:** Diverse denominations with different health-related beliefs and practices.
   - **Spiritual Support:** Importance of prayer and pastoral care, especially in hospital settings.
4. **Sikhism:**

- **Hair Removal:** Prohibitions against cutting hair (Kesh) can affect surgical preparations and certain medical tests. Even accessing scalp veins during emergency would be a sensitive matter if due explanation is not given *a-priore*.
- **Dietary Practices:** Some Sikhs are vegetarian, influencing dietary accommodations in healthcare settings.

5. **Jainism:**
    - **Strict Vegetarianism:** Refusal of medications containing animal products Ex – Gelatin containing capsules.
    - **Non-Violence:** Concerns about treatments harming microorganisms and other life forms.
6. **Buddhism:**
    - **End-of-Life Care:** Emphasis on mindfulness and consciousness at the time of death, affecting decisions about life support and pain medication.
7. **Black magic and witch craft believers** of any religion can disturb medical care and interfere with their rituals even in hospital settings for admitted patients.
8. **Cultural Practices:**
    - **Traditional Medicine:** Use of Ayurveda, Siddha, Unani, and homeopathy, which may conflict with allopathic treatments.
    - **Belief in Karma and Reincarnation:** Influences perceptions of suffering and disease.
    - Traditional but medically unacceptable practices like pre electrical feeds example honey, animal milk for infants, cowdung application on umbilical stump cause serious health hazards
9. **Gender Sensitivity:**
    - In many Indian cultures, modesty and gender roles can affect interactions with healthcare providers and decisions about medical procedures.
    - With the law enforcement, antenatal sex determination has been curtailed; but post natal sex discrimination and preferential medical care for the male child or infant is yet to be addressed.
10. **Language and Communication:**
    - India's linguistic diversity means that language barriers can impact understanding and consent in medical settings.
11. **Socioeconomic Factors:**
    - Economic constraints and caste-related issues can influence access to healthcare and adherence to treatments.
12. **Mental Health Stigma:**

- Cultural stigma associated with mental health issues can lead to underreporting and undertreatment.

13. **Family Involvement:**
    - Decision-making in Indian families is often collective, involving multiple family members.
14. **Healthcare Provider Sensitivity:**
    - Need for healthcare providers to be aware of and sensitive to these diverse beliefs and practices.
15. **Legal and Ethical Considerations:**
    - Balancing cultural sensitivity with medical ethics and legal obligations, especially in cases of child health, gender rights, and life-saving interventions.

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5.b. Conditions where palliative care is indicated in pediatrics

- ❖ Palliative care in pediatrics is a specialized medical approach aimed at improving the quality of life for children with serious illnesses
- ❖ It focuses on providing relief from the symptoms, pain, and stress of a serious illness, regardless of the diagnosis
- ❖ The goal is to improve quality of life for both the child and the family
- ❖ Pediatric palliative care is appropriate at any stage of a serious illness and can be provided alongside curative
- ❖ In pediatric palliative care, the approach is not only about extending life but also about enhancing the quality of life for the child and their family
- ❖ It involves a multidisciplinary team approach, including physicians, nurses, social workers, psychologists, and other healthcare professionals, working together to provide comprehensive care
- ❖ The care plan is tailored to the individual needs of the child and the family, taking into account their wishes, beliefs, and cultural backgrounds.

Conditions where palliative care can be considered:

1. **Cancer:**
    - Children with various types of cancer, including leukemia, brain tumors, and advanced solid tumors, often benefit from palliative care to manage pain, side effects, and emotional distress.
2. **Congenital Anomalies:**

- Conditions present at birth, such as severe congenital heart defects, trisomy 13 or 18, and spina bifida, where the focus is on enhancing quality of life and comfort.

3. **Neurological Disorders:**
    - Progressive neurodegenerative conditions like Duchenne Muscular Dystrophy, Batten disease, and severe cerebral palsy, where palliative care addresses pain, mobility issues, and feeding difficulties.
4. **Chronic Respiratory Conditions:**
    - Diseases like cystic fibrosis and severe bronchopulmonary dysplasia, where palliative care can help manage respiratory distress, frequent infections, and associated symptoms.
5. **Severe Genetic Disorders:**
    - Conditions such as Tay-Sachs disease, certain chromosomal abnormalities, and mitochondrial disorders, where palliative care focuses on symptom management and family support.
6. **End-Stage Organ Failure:**
    - Including end-stage renal disease, liver failure, and heart failure, where palliative care helps in managing symptoms, decision-making about treatment options, and end-of-life care.
7. **Metabolic Disorders:**
    - Incurable metabolic disorders like certain lysosomal storage diseases, where palliative care assists in managing symptoms and complications.
8. **Severe Neuromuscular Disorders:**
    - Conditions like advanced spinal muscular atrophy, where palliative care addresses mobility issues, respiratory support, and nutritional challenges.
9. **HIV/AIDS:**
    - In cases of advanced HIV/AIDS, palliative care can help manage symptoms, opportunistic infections, and psychosocial aspects of the disease.
10. **Complex Chronic Conditions:**
    - Children with multiple chronic conditions that lead to significant functional impairment, frequent hospitalizations, and complex care needs.
11. **Life-Limiting Traumatic Injuries:**
    - Severe injuries resulting in conditions like anoxic brain injury, where palliative care focuses on comfort and family support.
12. **Intractable Pain Syndromes:**

- Conditions where pain is a predominant feature and difficult to control, such as certain rheumatologic conditions.

13. **Severe Psychiatric Disorders:**
    - In rare cases, severe psychiatric disorders with significant impact on quality of life may also benefit from a palliative approach, particularly in terms of symptom management and family support.
14. **End-of-Life Care:**
    - When curative or life-prolonging treatments are no longer effective or desired, palliative care becomes central to providing comfort and dignity at the end of life.

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6.a. Indications for STI screening in sexually abused child

- ❖ Screening for sexually transmitted infections (STIs) in a child who has been sexually abused is a critical component of medical evaluation and care
- ❖ The decision to screen for STIs in these cases is based on several factors, including the type of abuse, the age of the child, symptoms, and the likelihood of specific infections
- ❖ It's important to approach STI screening in the context of sexual abuse with sensitivity and care, ensuring that the child's physical and psychological well-being is the primary focus
- ❖ The screening should be conducted in a manner that is age-appropriate and minimally invasive
- ❖ Collaboration with child protection services, mental health professionals, and legal authorities is often necessary to ensure comprehensive care and support for the child.

1. **Type of Sexual Abuse:**
    - Any history of penetrative sexual abuse, particularly involving genital or anal contact, warrants STI screening.
    - Non-penetrative abuse may also necessitate screening, depending on the nature of the contact and the likelihood of transmission.
2. **Symptoms Suggestive of STIs:**
    - Presence of symptoms such as genital discharge, sores, ulcers, warts, or other lesions in the genital area.
    - Symptoms of urinary tract infection or lower abdominal pain, which might indicate a sexually transmitted infection.

3. **Age and Pubertal Status:**
    - Adolescents are at a higher risk of having been sexually active and thus may have a higher risk of STIs.
    - Prepubertal children with a history of abuse also require screening, though the prevalence of STIs in this group is generally lower.
4. **Known STI in the Perpetrator:**
    - If the perpetrator is known to have an STI, screening the child for that specific infection is crucial.
5. **Forensic Evidence:**
    - If forensic evidence (such as semen or saliva) is found on the child's body or clothing, screening for STIs is indicated.
6. **High-Risk Sexual Abuse:**
    - Abuse involving multiple perpetrators, commercial sexual exploitation, or trafficking increases the risk of STIs and warrants comprehensive screening.
7. **Delayed Disclosure or Presentation:**
    - In cases where there is a significant delay between the time of abuse and the time of disclosure or presentation for care, screening is important as symptoms may not be present or may have resolved.
8. **Absence of Symptoms:**
    - Asymptomatic children who have been sexually abused should still be screened for STIs because many STIs can be asymptomatic, especially in the early stages.
9. **Local Prevalence and Epidemiology:**
    - Consideration of the local prevalence of specific STIs can guide screening decisions.
10. **Guidelines and Protocols:**
    - Adherence to local or national guidelines for the evaluation and treatment of sexually abused children, which often include recommendations for STI screening.
11. **Parental or Guardian Consent:**
    - Obtaining appropriate consent for screening, while ensuring the child's best interests and confidentiality.
12. **Follow-Up Screening:**
    - Some STIs have window periods say for example 6 weeks for HIV, where initial testing may be negative. Follow-up screening is often recommended several weeks to months after the initial evaluation.

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6.b. Lab investigations and Classifications of Anemia

Laboratory Investigations for Anemia:

1. **Complete Blood Count (CBC):**
   - **Hemoglobin (Hb) and Hematocrit (Hct):** Primary indicators of anemia.
   - **Red Blood Cell Indices:** Including mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC).
   - **Red Blood Cell Distribution Width (RDW):** Indicates variation in red cell size.
2. **Peripheral Blood Smear:**
   - Assessing RBC morphology, size, shape, and color.
   - Presence of abnormal cells or inclusions.
3. **Reticulocyte Count:**
   - Measures young RBCs in blood; indicates bone marrow response.
4. **Iron Studies:**
   - Serum iron, ferritin, total iron-binding capacity (TIBC), and transferrin saturation.
   - Useful in diagnosing iron deficiency anemia.
5. **Vitamin B12 and Folate Levels:**
   - Assessing for deficiencies leading to megaloblastic anemia.
6. **Direct Coombs Test (Direct Antiglobulin Test):**
   - Detects antibodies against RBCs, indicative of immune hemolytic anemias.
7. **Liver and Kidney Function Tests:**
   - Assessing organ function that can affect anemia.
8. **Hemoglobin Electrophoresis:**
   - Identifies abnormal hemoglobin variants (e.g., sickle cell, thalassemia).
9. **Bone Marrow Examination:**
   - In cases where the cause of anemia is not clear or when a bone marrow disorder is suspected.

Classification of Anemia:

1. **Based on MCV (Mean Corpuscular Volume):**
   - **Microcytic Anemia (MCV < 80 fL):** Iron deficiency, thalassemia, anemia of chronic disease.
   - **Normocytic Anemia (MCV 80-100 fL):** Acute blood loss, hemolysis, anemia of chronic disease, renal disease.

- **Macrocytic Anemia (MCV > 100 fL):** Vitamin B12 or folate deficiency, liver disease, alcoholism, hypothyroidism.

2. **Based on Etiology:**
   - **Nutritional Anemia:** Iron, B12, folate deficiencies.
   - **Hemolytic Anemia:** Sickle cell disease, G6PD deficiency, autoimmune hemolysis.
   - **Anemia of Chronic Disease:** Chronic infections, inflammation, malignancy.
   - **Aplastic Anemia:** Bone marrow failure syndromes.
   - **Anemia due to Chronic Kidney Disease:** Erythropoietin deficiency.
3. **Based on Pathophysiology:**
   - **Increased Red Blood Cell Loss:** Hemorrhagic anemia, hemolysis.
   - **Decreased Red Blood Cell Production:** Iron, B12, folate deficiencies, bone marrow suppression.
   - **Dysfunctional Red Blood Cell Production:** Thalassemia, sideroblastic anemia.
4. **Based on Bone Marrow Response:**
   - **Regenerative Anemia:** High reticulocyte count, indicating active bone marrow response.
   - **Non-regenerative Anemia:** Low reticulocyte count, indicating inadequate bone marrow response.

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7.a. Cough/ difficulty breathing classification as per IMNCI

SIGNS	CLASSIFY AS	IDENTIFY TREATMENT (Urgent pre-referral treatments are in bold print)
• Any general danger sign or • Chest indrawing or • Stridor in calm child	**SEVERE PNEUMONIA OR VERY SEVERE DISEASE**	▸ **Give first dose of Cotrimoxazole** ▸ **Refer URGENTLY to hospital**
• Fast breathing	**PNEUMONIA**	▸ **Give Cotrimoxazole for 5 days.** ▸ Soothe the throat and relieve the cough with a safe remedy. ▸ Advise mother when to return immediately. ▸ Follow-up in 2 days.
• No signs of pneumonia or very severe disease.	**NO PNEUMONIA: COUGH OR COLD**	▸ If coughing more than 21 days, refer for assessment. ▸ Soothe the throat and relieve the cough with a safe remedy ▸ Advise mother when to return immediately. ▸ Follow-up in 5 days if not improving.

- The Integrated Management of Neonatal and Childhood Illness (IMNCI) guidelines provide a classification system for cough or difficulty breathing in children, aimed at identifying the severity of the condition and guiding appropriate treatment
- The IMNCI guidelines are designed to be simple and effective, allowing healthcare workers, even in low-resource settings, to make crucial decisions and save lives
- They emphasize the importance of quick and accurate assessment, appropriate treatment, and timely referral to higher-level care when necessary.

The classification is based on **age-specific** signs and symptoms:

IMNCI Classification for Cough or Difficulty Breathing:

For Children Aged 2 Months Up to 5 Years:

1. **Severe Pneumonia or Very Severe Disease:**
    - Child has any of the following signs:
        - Unable to drink or breastfeed.
        - Vomits everything.
        - Convulsions.
        - Lethargic or unconscious.
        - Stridor in a calm child.
        - Severe malnutrition.
    - **Action:** Urgent referral to a hospital after giving the first dose of an appropriate antibiotic and treatment for hypoxemia if present.
2. **Pneumonia:**
    - Fast breathing (age-specific respiratory rate):
        - Age 2 months up to 12 months: 50 breaths per minute or more.
        - Age 12 months up to 5 years: 40 breaths per minute or more.
    - No signs of severe pneumonia or very severe disease.
    - **Action:** Treat with an appropriate antibiotic for pneumonia.
3. **No Pneumonia (Cough or Cold):**
    - Cough or cold but does not have fast breathing or chest indrawing.
    - No signs of pneumonia or very severe disease.
    - **Action:** Home care advice, including instructions on when to return.

For Infants Aged 1 Week Up to 2 Months:

1. **Severe Pneumonia or Very Severe Disease:**
    - Any general danger sign (as above) or any of the following:
        - Severe chest indrawing.
        - Nasal flaring.
        - Grunting.
    - **Action:** Urgent referral to a hospital with the first dose of an appropriate antibiotic.
2. **Pneumonia:**
    - Fast breathing (respiratory rate 60 breaths per minute or more).
    - No signs of severe pneumonia or very severe disease.
    - **Action:** Treat with an appropriate antibiotic for pneumonia.
3. **No Pneumonia (Cough or Cold):**
    - Mild illness without any of the above signs.
    - **Action:** Home care advice and instructions on when to return.

Notes:

- **Respiratory Rate Counting:** Accurate counting of respiratory rates for a full minute is crucial. If tachypnea for the age is detected then it has to be counted on three different minutes for full 1 minute each time and average of the three readings has to be taken for definition of fast breathing.
- **Assessment of Other Symptoms:** Look for other symptoms or diseases that may need treatment.
- **Follow-Up:** Advising caregivers on when to return for follow-up or if the child's condition worsens.
- **Prevention:** Education on preventive measures, including vaccination and environmental factors.

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7.b. WHO classification of Dehydration

- The World Health Organization (WHO) classifies dehydration in children primarily based on clinical assessment
- This classification is crucial for determining the severity of dehydration and guiding appropriate treatment, especially in settings where laboratory tests may not be readily available

- This classification system is widely used in global health, particularly in resource-limited settings, and forms a part of the Integrated Management of Childhood Illness (IMCI) guidelines

- ❖ It emphasizes the importance of early recognition and treatment of dehydration to prevent morbidity and mortality in children.
- ❖ *The classification is divided into three categories: no dehydration, some dehydration, and severe dehydration.*

WHO Classification of Dehydration:

1. **No Dehydration:**
   - Symptoms:
     - Alert, well, normal thirst.
     - Eyes not sunken.
     - Mouth and tongue moist.
     - Tears present.
     - Normal skin turgor (skin pinch goes back quickly).
     - Normal urine output.
   - Management:
     - Continue feeding.
     - Increase fluid intake.
     - Monitor for any signs of worsening.
2. **Some Dehydration:**
   - Symptoms:
     - Restless or irritable.
     - Sunken eyes.
     - Dry mouth and tongue.
     - Thirsty, drinks eagerly.
     - Reduced tears.
     - Skin pinch goes back slowly.
     - Possibly reduced urine output.
   - Management:
     - Oral Rehydration Solution (ORS).
     - Continue feeding.
     - Frequent monitoring.
     - If unable to drink or persistent vomiting, seek medical attention.
3. **Severe Dehydration:**
   - Symptoms:
     - Lethargic or unconscious.
     - Very sunken eyes.
     - Very dry mouth and tongue.
     - Drinks poorly or unable to drink.

- Absent tears.
- Skin pinch goes back very slowly.
- Significantly reduced or absent urine output.

- Management:
  - Urgent medical attention.
  - Intravenous fluids.
  - Close monitoring and supportive care.
  - Continue feeding as soon as possible.

Imp points:

- **Assessment:** The classification is based on a combination of signs and symptoms. It's important to assess the overall clinical picture rather than relying on a single sign.
- **Fluid Replacement:** The choice between oral rehydration solution (ORS) and intravenous fluids depends on the severity of dehydration and the child's ability to drink.
- **Monitoring:** Regular monitoring of hydration status, especially in the case of some dehydration, is crucial to prevent progression to severe dehydration.
- **Prevention:** Education on preventive measures, including proper hygiene, safe drinking water, and timely treatment of diarrheal illnesses, is important.

Classification	Symptoms	Management
No Dehydration	Alert, well, normal thirst Eyes not sunken Mouth and tongue moist Tears present Normal skin turgor (quick skin pinch return) Normal urine output	Continue feeding Increase fluid intake Monitor for any signs of worsening
Some Dehydration	Restless or irritable Sunken eyes Dry mouth and tongue Thirsty, drinks eagerly Reduced tears Skin pinch goes back slowly Possibly reduced urine output	Oral Rehydration Solution (ORS) Continue feeding Frequent monitoring Seek medical attention if unable to drink or persistent vomiting
Severe Dehydration	Lethargic or unconscious Very sunken eyes	Urgent medical attention Intravenous fluids

	Very dry mouth and tongue Drinks poorly or unable to drink Absent tears Skin pinch goes back very slowly Significantly reduced or absent urine output	Close monitoring and supportive care Continue feeding as soon as possible

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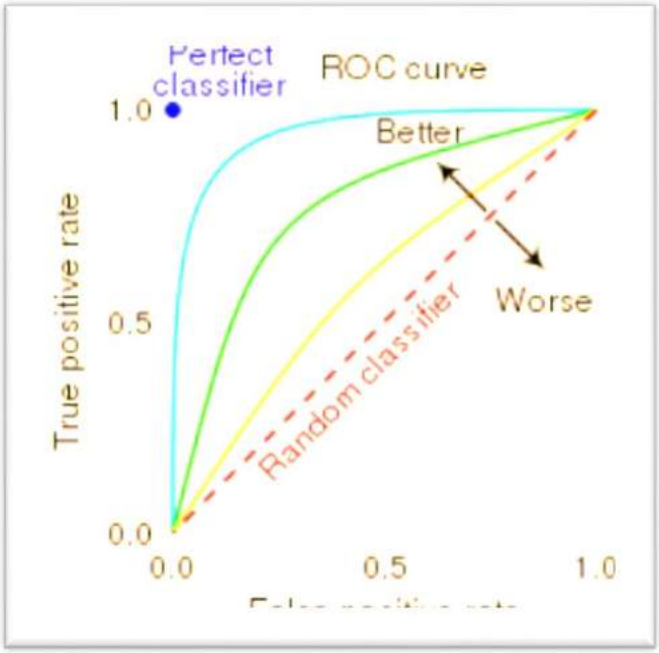
8.a. ROC and AUC

- ROC and AUC are valuable in pediatric research for quantifying the accuracy of diagnostic tests and models
- They help in identifying the most effective tools for early detection and intervention, which is crucial in pediatrics where early treatment can significantly impact a child's health and development trajectory.

ROC Curve:

- **Definition:** A ROC curve is a graphical plot that illustrates the diagnostic ability of a binary classifier system as its discrimination threshold is varied.
- **Two Axes:** ROC plots true positive rate (sensitivity) against false positive rate (1-specificity).
- **X-axis:** Represents the false positive rate (1 - Specificity).
- **Y-axis:** Represents the true positive rate (Sensitivity).

- **Purpose:** To visualize the trade-off between sensitivity and specificity for every possible cut-off.



- **True Positive Rate (Sensitivity):** Proportion of actual positives correctly classified by the model.
- **False Positive Rate (1-Specificity):** Proportion of actual negatives incorrectly classified as positives by the model.
- **Perfect Classifier:** A perfect classifier's ROC curve goes straight up the y-axis and then straight across the x-axis.
- **Random Classifier:** A random classifier's ROC curve is a diagonal line from the bottom left to the top right.
- **Model Assessment:** The closer the curve is to the top left corner, the better the model's performance.

AUC:

- **Definition:** The AUC represents the area under the ROC curve.
- **Purpose:** To provide a single measure of how well a test can distinguish between two diagnostic groups.
- **Interpretation:**
    - AUC measures the overall performance of a model.
    - AUC = 0.5 for a random classifier, AUC = 1 for a perfect classifier.

- Higher AUC indicates better discrimination ability.
    - **0.5:** No diagnostic ability (equivalent to random guessing).
    - **0.5 - 0.7:** Poor diagnostic ability.
    - **0.7 - 0.9:** Moderate diagnostic ability.
    - **>0.9:** High diagnostic ability.

Application in Pediatric Research:

- In pediatric research, ROC and AUC are used to evaluate the effectiveness of diagnostic tests, screening tools, or predictive models.
- For example, in developing a new screening tool for autism in children, researchers might use the ROC curve to determine the sensitivity and specificity of the tool at various threshold levels.
- The AUC would then give an overall measure of the tool's effectiveness.

Example:

- **Study Objective:** To develop a screening tool for early detection of developmental delays in children.
- **Method:** Researchers collect data on various developmental parameters and outcomes from a pediatric population.
- **ROC Analysis:** They plot a ROC curve for each parameter to see how well it predicts developmental delay.
- **AUC Calculation:** The AUC for each parameter is calculated to determine its overall predictive power.
- **Outcome:** Parameters with higher AUC values are considered more effective for inclusion in the screening tool.

The ROC curve and AUC are valuable tools for assessing the performance of binary classification models, especially in medical diagnostics.
They provide insights into a model's ability to discriminate between classes across different decision thresholds.

- **Comparing Models:** When comparing two models, the one with the higher AUC is generally better.
- **Choosing Thresholds:** Depending on the situation, you might prioritize sensitivity over specificity or vice versa, influencing the threshold choice.

- **Clinical Application:** Commonly used in medical fields to evaluate diagnostic tests like medical imaging, blood tests, etc.
- **Limitations:**
    - AUC doesn't show how well a model will perform at a specific threshold.
    - ROC might be less informative when dealing with imbalanced datasets.

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8.b. Type 1 and 2 errors in statistics

- **Type I Error (False Positive):**
    - Occurs when a true null hypothesis is incorrectly rejected.
    - Represents a false alarm; for example, concluding a treatment is effective when it is not effective in reality.
    - The probability of making a Type I error is denoted by the alpha level (α), commonly set at 0.05, indicating a 5% risk of this error.

Alpha Error (Type I Error) - False Positive:

- **Definition:** Occurs when the null hypothesis (no difference or effect) is incorrectly rejected in favor of the alternative hypothesis.
- **Clinical Implication:**
    - Leads to the assumption that a treatment or intervention is effective when it is not.
    - In pediatrics, this could mean adopting a new drug or therapy that does not genuinely improve patient outcomes, potentially exposing children to unnecessary risks or side effects.

Type 1 error - Practical Example in Research:

- **Study Objective:** Research investigating the effectiveness of a new drug to treat pediatric asthma.
- **Null Hypothesis:** The new drug is not more effective than the existing standard treatment.
- **Result:** The study concludes that the new drug is significantly more effective than the standard treatment.

- **Type 1 Error Occurrence:** If, in reality, the new drug is not more effective and the study's conclusion is incorrect, this represents a Type 1 error. The study falsely indicates a benefit where none exists, potentially leading to the unnecessary use of a new drug with unknown long-term effects in children.

    - **Control Methods:**
        - Set a lower alpha level (e.g., 0.01 instead of 0.05) in studies with potentially high risks or in multi-arm trials to reduce the probability of this error.
        - Use Bonferroni correction for multiple comparisons to adjust the significance level and reduce the chance of this error.
    - **Alpha Level in Clinical Studies:**
        - Typically set at 0.05, implying a 5% chance of concluding a treatment is effective when it is not.
        - The choice of alpha level can be more conservative in pediatric studies due to the vulnerable nature of the population.

Beta Error (Type II Error) - False Negative:

- Happens when a false null hypothesis is not rejected.
- This error leads to missing a genuine effect or difference; for example, failing to recognize the efficacy of a beneficial treatment.
- The risk of Type II error is denoted by beta (β), and power of a study (1-β) reflects the probability of correctly rejecting a false null hypothesis.

- **Type II Error (False Negative):**
    - **Definition:** Occurs when a false null hypothesis is not rejected, meaning a real effect or difference is missed by the researcher but it actually existed.
    - **Clinical Implication:**
        - Results in the failure to identify a beneficial treatment or intervention.
        - In pediatric practice, this could delay the adoption of new, effective treatments or lead to the continued use of less effective ones.

Type 2 error - Practical Example in Research:

- ***Study Objective:*** Research evaluating the impact of a special diet on children with ADHD (Attention Deficit Hyperactivity Disorder).
- ***Null Hypothesis:*** The special diet has no effect on ADHD symptoms in children.
- ***Result:*** The study concludes that there is no significant effect of the diet on ADHD symptoms.
- ***Type 2 Error Occurrence:*** If, in reality, the special diet does have a beneficial effect on ADHD symptoms, but the study fails to detect this effect, it represents a Type 2 error. The study incorrectly suggests that the diet is ineffective, possibly leading to the dismissal of a potentially beneficial intervention for children with ADHD.

- **Power of the Study:**
    - The power (1 - beta) is the probability of correctly rejecting a false null hypothesis.
    - High power is required to ensure reliable detection of true effects, especially in pediatrics, where patient numbers may be limited, and effects subtle.
- **Determinants of Power:**
    - Sample size: Larger samples increase power.
    - Effect size: Larger effect sizes increase power.
    - Variability: Lower variability in data increases power.
    - Alpha level: Setting a higher alpha level can increase power but also increases the risk of a Type I error.
- **Balancing Alpha and Beta in Clinical Research:**
    - **Trade-Off:** Increasing power (decreasing beta) can increase the chance of a Type I error if the alpha level is not adjusted.
    - **Clinical Trials:**
        - In pediatric trials, careful consideration is required to balance these errors, ensuring that new treatments are neither adopted prematurely based on false positives nor rejected incorrectly due to false negatives.

- **Application in Clinical Decision Making:**
    - **Evidence-Based Practice:**
        - Understanding these errors aids in critically evaluating research for evidence-based practice.
        - Clinicians can better assess the reliability of study results and make informed decisions about integrating research findings into pediatric care.

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9.a. QRS in ECG - normal and abnormal

- Pediatric ECG interpretation requires an understanding of the developmental changes in cardiac physiology.
- Abnormalities in the QRS complex can be subtle and should be interpreted in the context of the child's overall health, symptoms, and clinical history.

Normal QRS Complex in Pediatrics:

1. **Newborns (0-1 month):**
    - Duration: 60-80 milliseconds.
    - Axis: Rightward (typically +110° to +180°).
    - R Wave: Prominent in right precordial leads (reflecting right ventricular dominance).
2. **Infants (1-12 months):**
    - Duration: 70-90 milliseconds.
    - Axis: Gradual shift leftward.
    - R Wave: Decreasing dominance in right precordial leads.
3. **Children (1-6 years):**
    - Duration: 70-100 milliseconds.
    - Axis: Normal axis -5° to +110°.

- R Wave: Further decrease in right precordial leads; S wave deepens in left precordial leads.

4. **Older Children and Adolescents (6-16 years):**
    - Duration: 80-100 milliseconds.
    - Axis: Normal adult pattern (-30° to +90°).
    - R Wave: Adult-like pattern; R wave height increases in left precordial leads.

Abnormal QRS Complex:

1. **Prolonged QRS Duration:**
    - 100 milliseconds in children and adolescents.
    - Indicates possible bundle branch block, ventricular hypertrophy, or pre-excitation.
2. **Abnormal Axis:**
    - Extreme right axis deviation (>+180°) or left axis deviation (<-30°).
    - Suggests underlying heart disease, such as congenital defects.
3. **Abnormal R Wave Progression:**
    - Poor R wave progression in precordial leads.
    - May indicate anterior myocardial damage or abnormal ventricular conduction.
4. **Abnormal Q Waves:**
    - Significant Q waves in lateral or inferior leads.
    - Can be a sign of myocardial infarction (rare in children) or myocardial scarring.
5. **Increased QRS Voltage:**
    - Significantly high R waves in precordial leads.
    - Suggests ventricular hypertrophy.
6. **Low Voltage QRS:**
    - Decreased overall QRS amplitude.

- May indicate pericardial effusion or myocardial disease.

Clinical Pediatric Considerations:

- **Growth and Development:** The heart's electrical system and the chest's physical structure change as children grow, affecting ECG readings.
- **Congenital Heart Disease:** Children with congenital heart disease may have unique ECG patterns.
- **Symptomatic Evaluation:** Any abnormal findings in a pediatric ECG, especially if associated with symptoms, should be evaluated further.

Abnormal QRS Feature	Possible Pediatric Interpretation	Associated Pediatric Conditions
Prolonged Duration	Delayed ventricular depolarization	Bundle branch blocks, congenital heart disease, cardiomyopathies, electrolyte imbalances
Abnormal Q Waves	Myocardial damage or scarring	Congenital heart disease (e.g., ventricular septal defect), myocarditis, cardiomyopathies
Increased Amplitude	Enlarged ventricular mass	Ventricular hypertrophy (due to congenital heart disease or hypertension), athletic heart syndrome in adolescents
Abnormal Axis	Altered cardiac position or conduction	Congenital heart disease (e.g., atrial septal defect), abnormal cardiac position (e.g., dextrocardia), lung diseases
Abnormal Morphology	Abnormal electrical pathways or origins	Pre-excitation syndromes (e.g., Wolff-Parkinson-White syndrome), ventricular tachycardia, post-operative changes in congenital heart disease
QRS Alternans	Electrical instability	Rare in pediatrics, but can be seen in severe myocardial disease or pericardial effusion
Low Voltage QRS	Decreased electrical activity	Pericardial effusion, myocarditis, hypothyroidism, large pleural effusion

Rightward Axis	Right ventricular dominance	Normal in newborns and infants, pulmonary pathology, congenital heart disease (e.g., Tetralogy of Fallot)
Leftward Axis	Left ventricular dominance	Less common in pediatrics, may be seen in conditions like congenital heart block or left ventricular hypertrophy

Imp Points:

- **Age-Related Variations:** The QRS complex in children can vary with age. For instance, a rightward axis is common in infants and young children due to the physiological right ventricular dominance.
- **Congenital Heart Disease:** Many abnormalities in the QRS complex in children can be indicative of congenital heart disease, necessitating further investigation.
- **Electrolyte Imbalances:** In children, especially those with chronic conditions or on certain medications, electrolyte imbalances can significantly affect the QRS complex.

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9.b. Fetal, transitional and neonatal circulation

Definitions and general charecterstics:

Fetal Circulation:

- **Characteristics:**
  - **Oxygenation via Placenta:** The fetus receives oxygenated blood from the mother through the placenta.
  - **Shunts in Circulation:** Three main shunts - the ductus venosus, foramen ovale, and ductus arteriosus - bypass non-functional fetal lungs and liver.
  - **High Pulmonary Vascular Resistance:** Due to fluid-filled lungs and low oxygen tension, causing minimal blood flow to the lungs.
- **Key Components:**
  - **Ductus Venosus:** Shunts a portion of blood from the umbilical vein directly to the inferior vena cava, bypassing the liver.
  - **Foramen Ovale:** An opening between the right and left atria, allowing blood to flow directly from the right to the left atrium.
  - **Ductus Arteriosus:** Connects the pulmonary artery to the descending aorta, diverting blood away from the lungs.

Transitional Circulation:

- **Transition Phase:**

- **Occurs at Birth:** Initiated by the infant taking the first breath, leading to significant physiological changes.
- **Closure of Shunts:** The foramen ovale, ductus arteriosus, and ductus venosus begin to close.
- **Decrease in Pulmonary Vascular Resistance:** Expansion and aeration of the lungs reduce pulmonary resistance, increasing blood flow to the lungs.

- **Adaptations:**
  - **Increased Pulmonary Blood Flow:** More blood is directed to the lungs for oxygenation.
  - **Functional Closure of Shunts:** The foramen ovale and ductus arteriosus functionally close due to changes in pressure gradients and oxygen levels.

Neonatal Circulation:

- **Established Post-Birth:**
  - **Fully Functional Lungs:** The neonate's lungs are now responsible for oxygenation.
  - **Closure of Fetal Shunts:** The ductus arteriosus and foramen ovale usually close completely within the first few days to months of life.
  - **Normal Adult Circulation Pattern:** Blood flows to the lungs for oxygenation and then is distributed to the rest of the body.
- **Physiological Changes:**
  - **Increased Oxygen Saturation:** Higher oxygen levels in the blood due to lung function.
  - **Normal Cardiac Output Distribution:** Blood is evenly distributed between the systemic and pulmonary circulations.

A. Fetal Circulation

1. Placental Gas Exchange: In utero, oxygen and nutrients are supplied to the fetus via the placenta. The fetal lungs are non-functional, and the liver plays a minor role in metabolic functions.

2. Umbilical Cord: The umbilical cord contains two arteries and one vein. Oxygenated blood and nutrients are transported from the placenta to the fetus via the umbilical vein, while deoxygenated blood and waste products are carried away by the umbilical arteries.

3. Ductus Venosus: In the fetal liver, blood flows through the ductus venosus, which shunts a portion of oxygenated blood directly into the inferior vena cava, bypassing the liver.

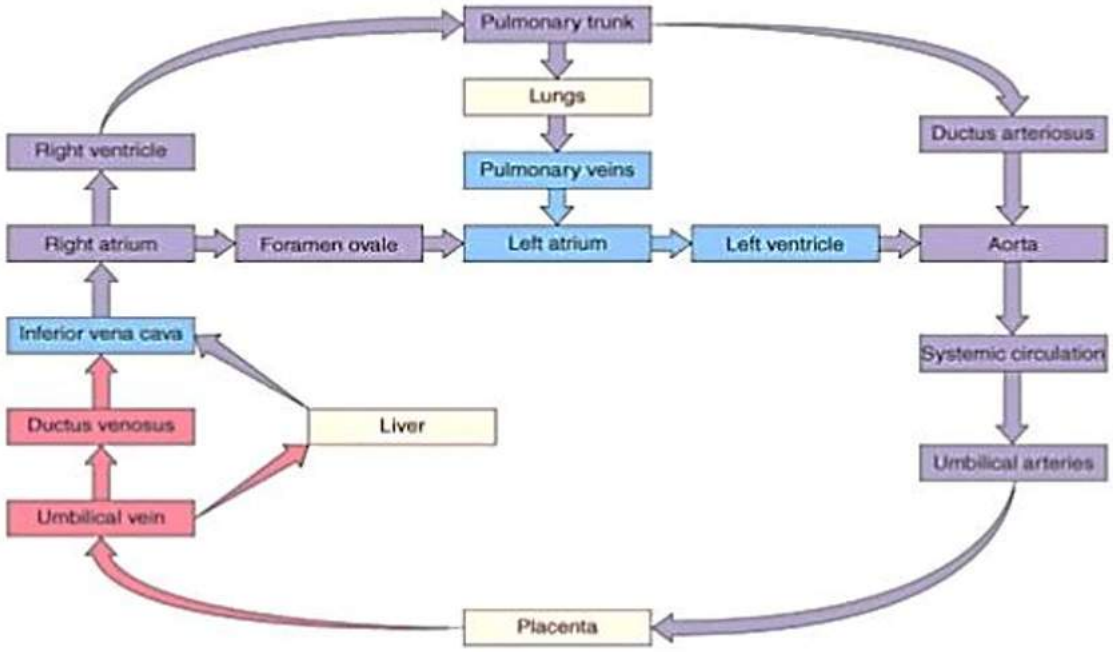
4. Foramen Ovale: Blood entering the right atrium is directed through the foramen ovale, a hole in the atrial septum, into the left atrium. This bypasses the non-functional fetal lungs.

5. Ductus Arteriosus: Blood from the right ventricle is pumped into the pulmonary artery but is shunted away from the lungs through the ductus arteriosus and into the aorta. This further ensures that most of the blood bypasses the lungs.

6. Umbilical Blood Oxygenation: Oxygenated blood from the placenta mixes with deoxygenated blood in the right atrium but is mostly directed towards the foramen ovale, preserving a higher oxygen content.

7. **Pulmonary Arteries**: Carry a small amount of blood to the lungs for nourishment, but not for oxygen exchange.

8. Umbilical Arteries: Return deoxygenated blood and waste products from the fetus to the placenta.



B. Cardiovascular Adjustments After Birth

The transition from fetal to postnatal circulation involves several critical changes that occur in response to the first breath and the increase in oxygen levels.

1. Lung Expansion: The first breath taken by the newborn triggers lung expansion. This leads to an increase in pulmonary vascular resistance and a decrease in systemic vascular resistance due to increased oxygen in the lungs.

2. Closure of Foramen Ovale: The pressure in the left atrium exceeds that in the right atrium as a result of lung expansion and oxygenation. This pressure difference forces the septum primum against the septum secundum, closing the foramen ovale.

3. Closure of Ductus Arteriosus: Increased oxygen levels cause the muscular wall of the ductus arteriosus to contract, gradually closing off this vessel. Closure is typically complete within the first few days of life.

4. Ductus Venosus Closure: With the interruption of umbilical blood flow, the ductus venosus constricts and eventually closes.

5. Liver Function: As the newborn begins to rely on the gastrointestinal tract for nutrient absorption, liver function increases, and the liver gradually takes on its metabolic role.

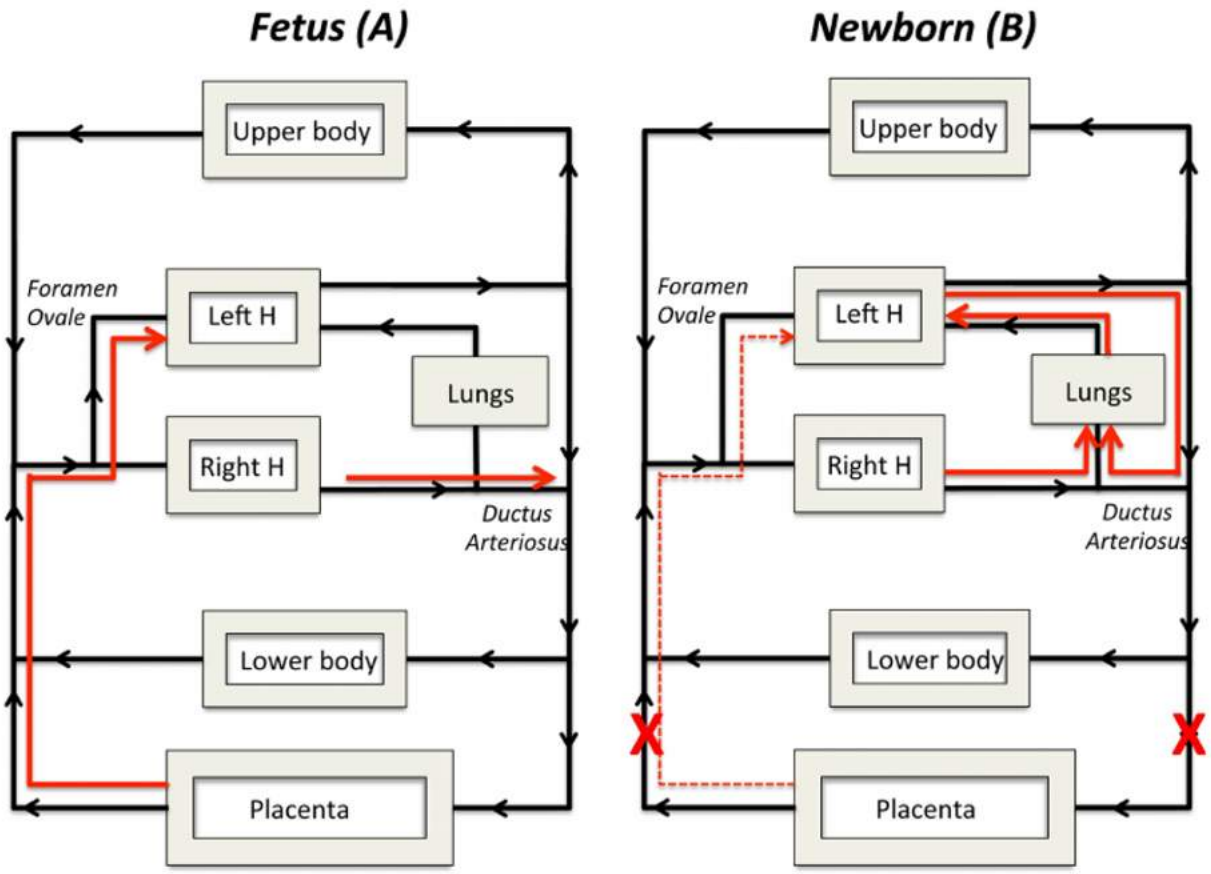
6. Systemic Blood Flow: The systemic circulation adapts to the increased oxygen content, and the neonate's systemic blood flow becomes independent of umbilical circulation.

7. Maintenance of Umbilical Blood Flow: In some cases, the umbilical arteries and ductus venosus may remain patent for a short period, but they gradually close within a few days to weeks after birth.

8. Changes in Circulation: The heart and circulatory system start functioning independently. The right side of the heart pumps deoxygenated blood to the lungs, and the left side pumps oxygenated blood to the rest of the body.

9. Degeneration of Umbilical Vessels: The umbilical vein and arteries close and eventually become ligamentous structures (round ligament of the liver and umbilical ligaments).

10. Continued Maturation: Over the first few weeks to months, the cardiovascular system continues to mature, and circulation becomes similar to that of an adult.



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10.a. Red flags signs for development assessment

- Red flag signs in developmental assessment are critical indicators that suggest a child may be at risk for developmental delays or disorders.
- Recognizing these signs early is crucial for timely intervention and support.
- **Early Detection is Key:** Recognizing these red flags early allows for timely referral to specialists, early intervention, and better outcomes.
- **Individual Variations:** It's important to note that children develop at different rates, and not meeting a specific milestone precisely on time isn't always a cause for concern. However, the presence of multiple red flags or a significant delay in any one area warrants further evaluation.

- **Holistic Approach:** Developmental assessment should be comprehensive, considering all areas of development and the child's environment and health history.

Red flag signs categorized by different developmental domains:

General Red Flags:

- No smiling by 3 months
- No social smile by 6 months
- No reaction to loud noises or no babbling by 6 months
- Inability to sit without support by 9 months
- No use of single words by 16 months
- No two-word spontaneous phrases by 24 months (excluding echoing or repeating)
- Loss of any language or social skills at any age

Motor Development:

- Persistent fisting or tight hand muscles beyond 3 months
- Asymmetry in movements (using one side of the body more than the other)
- Inability to bear weight on legs with support by 6 months
- Not rolling over by 6 months
- Inability to sit with support by 9 months
- Inability to crawl/ stand with support by 12 months
- Not walking with support by 15 months
- Not walking by 18 months
- Walking exclusively on toes

Language and Speech Development:

- Lack of vocalisation by 6 months of age
- Lack of cooing or babbling by 12 months
- Not responding to their name by 12 months
- Absence of pointing, showing, reaching, or waving by 12 months
- Absence of single words by 16 months
- Not following simple instructions by 24 months
- Poor eye contact
- Limited or no imitation of sounds or gestures

Social and Emotional Development:

- Doesn't wave bye-bye by 12 months
- Lack of interest in other children or caregivers
- Limited or no eye contact
- Does not seek attention or enjoy being cuddled
- Does not engage in pretend play
- Persistent preference for solitary play
- Extreme difficulty in calming down

Cognitive Development:

- Does not explore surroundings or play with toys in a functional manner
- Lack of curiosity or interest in new things
- Difficulty with problem-solving or logical thinking appropriate for age
- Significant delay in understanding cause and effect relationships

Sensory and Feeding:

- Overly sensitive to light, noise, textures, or temperatures
- Under-reactive to sensory stimulation
- Feeding difficulties (persistent problems with swallowing, chewing, or gagging)
- Excessive drooling or difficulties in controlling saliva beyond the age of 24 months

Behavioral:

- Excessive irritability or crying
- Unusually passive or unresponsive
- Repetitive unusual body movements (e.g., hand-flapping, rocking)
- Extreme resistance to change in routine or environment

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10.b. Screening tests for language disorders and ASD

Screening for Language Disorders:

1. **Ages and Stages Questionnaires (ASQ):**
   - Target Age: 1 month to 5½ years.
   - Focus: Broad developmental screening, including communication milestones.
   - Method: Parent-completed questionnaire.
2. **Communication and Symbolic Behavior Scales (CSBS):**

- Target Age: 6 to 24 months.
- Focus: Early identification of communication delays.
- Method: Parent questionnaire and direct child assessment.

3. **Preschool Language Scale (PLS):**
    - Target Age: Birth to 7 years.
    - Focus: Auditory comprehension and expressive communication skills.
    - Method: Interactive tasks and observations.
4. **Clinical Evaluation of Language Fundamentals - Preschool (CELF-Preschool):**
    - Target Age: 3 to 6 years.
    - Focus: Assessment of language fundamentals including morphology, syntax, and semantics.
    - Method: Standardized testing.

Screening for Autism Spectrum Disorder (ASD):

1. **Modified Checklist for Autism in Toddlers (M-CHAT):**
    - Target Age: 16 to 30 months.
    - Focus: Identifying risk of ASD in toddlers.
    - Method: Parent-completed questionnaire with follow-up interview if required.
2. **Ages and Stages Questionnaires: Social-Emotional (ASQ:SE):**
    - Target Age: 6 months to 6 years.
    - Focus: Social-emotional development, which can flag concerns related to ASD.
    - Method: Parent-completed questionnaire.
3. **Social Communication Questionnaire (SCQ):**
    - Target Age: 4 years and older.
    - Focus: Screening for communication and social functioning related to ASD.
    - Method: Parent questionnaire based on the Autism Diagnostic Interview-Revised.
4. **Autism Diagnostic Observation Schedule (ADOS):**
    - Target Age: Toddlers to adults.
    - Focus: Comprehensive assessment of communication, social interaction, and play.
    - Method: Semi-structured assessment by a trained professional.
5. **Screening Tool for Autism in Toddlers and Young Children (STAT):**
    - Target Age: 24 to 36 months.
    - Focus: Identifying autism in young children.
    - Method: Interactive assessment tasks.

Practical Considerations:

- **Early Identification:** Early screening and identification of language disorders and ASD are crucial for timely intervention.
- **Parental Involvement:** Many screening tools rely on parental reports, as parents are often the first to notice developmental concerns.
- **Professional Evaluation:** Screening tools are not diagnostic. If a screening tool indicates a risk, a comprehensive evaluation by a specialist (e.g., speech-language pathologist, developmental pediatrician, psychologist) is necessary.
- **Cultural Sensitivity:** Screening tools should be used with consideration of the child's cultural and linguistic background.

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Paper 2

1.a. Complication in infant of diabetic mother

- Infants born to diabetic mothers (IDMs) are at risk for a variety of complications, which can be related to maternal hyperglycemia during pregnancy.
- These complications can affect almost every system in the infant's body and can have both immediate and long-term consequences.

Metabolic Complications:

1. **Hypoglycemia:**
    - Infants of diabetic mothers have a high risk of developing hypoglycemia shortly after birth due to hyperinsulinemia.
    - Monitoring of blood glucose levels and early feeding or intravenous glucose may be necessary.
2. **Hypocalcemia and Hypomagnesemia:**
    - These electrolyte disturbances can occur secondary to maternal diabetes and may require supplementation.
3. **Hyperbilirubinemia:**
    - IDM are at increased risk for jaundice, which may necessitate phototherapy or even exchange transfusion in severe cases.

Cardiac Complications:

1. **Congenital Heart Defects:**

- The risk of cardiac anomalies, such as ventricular septal defects and transposition of the great arteries, is increased.

2. **Cardiomyopathy:**

- Hypertrophic cardiomyopathy, particularly of the interventricular septum, is more common and is associated with maternal hyperglycemia.

Respiratory Complications:

- **Respiratory Distress Syndrome (RDS):**

- Despite adequate gestational age, infants of diabetic mothers are at higher risk for RDS due to delayed lung maturity.

Growth Abnormalities:

1. **Macrosomia:**

- Excessive fetal growth is a common complication and can lead to delivery complications such as shoulder dystocia.

2. **Intrauterine Growth Restriction (IUGR):**

- In cases of vasculopathy associated with long-standing or poorly controlled diabetes, the infant may be at risk for IUGR.

Neurological Complications:

1. **Birth Injuries:**

- Due to macrosomia, there is an increased risk of birth trauma, which can result in injuries such as brachial plexus injury.

2. **Motor and Cognitive Development:**

- Long-term studies suggest that IDMs may have an increased risk of developmental delays.

Gastrointestinal Complications:

- **Small Left Colon Syndrome:**

- This condition can cause transient lower intestinal obstruction in IDMs.

Renal Complications:

- **Renal Vein Thrombosis:**

- IDM are at increased risk for renal vein thrombosis, which can be life-threatening.

Hematologic Complications:

- **Polycythemia:**
    - Secondary to chronic fetal hypoxia, IDMs may have an increased hematocrit, which can lead to hyperviscosity syndrome.

Endocrine Complications:

- **Risk of Developing Diabetes:**
    - There is a higher lifetime risk of the infant developing type 2 diabetes, especially if the maternal diabetes was poorly controlled.

Immunologic Complications:

- **Infections:**
    - IDMs may have an increased risk of infections, which necessitates careful monitoring.

Management of Complications:

- **Prenatal Care:**
    - Tight glycemic control during pregnancy to reduce the risk of complications.
    - Regular monitoring of fetal growth and well-being.
- **Delivery Planning:**
    - Consideration of the timing and mode of delivery to minimize the risk of birth trauma and other complications.
- **Postnatal Care:**
    - Immediate assessment and stabilization of the infant after birth.
    - Monitoring for and management of metabolic, respiratory, and other complications.

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1.b. Pathophysiology of IDM

1. Hyperglycemia and Insulin Response:

- **Maternal Hyperglycemia:** In a diabetic pregnancy, high levels of glucose in the mother's blood cross the placenta into the fetal circulation.
- **Fetal Hyperinsulinemia:** The fetus's pancreas responds to this high glucose level by producing more insulin (hyperinsulinemia).
- **Increased Insulin Effects:** Insulin acts as a growth factor, leading to macrosomia (large body size) and increased fat and muscle mass in the fetus.

2. **Macrosomia and Birth Complications:**
   - **Large Fetal Size:** The increased insulin stimulates excessive fetal growth, particularly in the form of fat.
   - **Birth Complications:** Macrosomia increases the risk of birth injuries, shoulder dystocia, and the need for cesarean delivery.
3. **Metabolic Disturbances After Birth:**
   - **Hypoglycemia:** After birth, the sudden discontinuation of the high glucose supply from the mother can lead to neonatal hypoglycemia, as the infant's pancreas continues to produce high levels of insulin.
   - **Hypocalcemia and Hypomagnesemia:** IDM is also at risk for low calcium and magnesium levels, possibly due to parathyroid suppression by maternal hyperglycemia.
4. **Respiratory Distress Syndrome (RDS):**
   - **Delayed Lung Maturity:** Insulin inhibits the production of surfactant, a substance necessary for lung function, leading to an increased risk of respiratory distress syndrome.
   - **Increased Risk in Preterm Infants:** This risk is particularly high if the infant is born preterm.
5. **Cardiomyopathy:**
   - **Hypertrophic Cardiomyopathy:** Excessive insulin can lead to hypertrophic cardiomyopathy, characterized by thickening of the heart muscle.
6. **Long-term Risks:**

- **Risk of Obesity and Diabetes:** Children born to diabetic mothers have a higher risk of developing obesity and type 2 diabetes later in life.
- **Potential Developmental Issues:** There may be an increased risk of developmental and cognitive issues, although this is still an area of ongoing research.

7. **Polycythemia and Hyperbilirubinemia:**
   - **Increased Red Blood Cell Production:** The fetus may produce more red blood cells in response to relative hypoxia caused by thickened blood (due to increased fetal size).
   - **Hyperbilirubinemia:** After birth, the breakdown of these excess red blood cells can lead to jaundice.

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1.c. Clinical features and management of IDM

Clinical Features of IDMs:

1. **Macrosomia:**
   - **Definition:** Birth weight >90th percentile for gestational age.
   - **Complications:** Increased risk of birth trauma, shoulder dystocia, and cesarean delivery.
2. **Hypoglycemia:**
   - **Timing:** Typically occurs within the first few hours to days of life.
   - **Mechanism:** Persistent hyperinsulinemia post-delivery with a sudden loss of maternal glucose supply.
   - **Symptoms:** Jitteriness, cyanosis, seizures, apnea, tachypnea, and poor feeding.
3. **Respiratory Distress Syndrome (RDS):**
   - **Incidence:** Higher in preterm IDMs.
   - **Mechanism:** Insulin inhibits surfactant production.
   - **Clinical Presentation:** Tachypnea, grunting, retractions, and cyanosis soon after birth.
4. **Cardiomyopathy:**
   - **Type:** Often hypertrophic, particularly of the interventricular septum.
   - **Clinical Significance:** Can lead to outflow tract obstruction and heart failure.

5. **Polycythemia and Hyperbilirubinemia:**
    - **Etiology:** Increased erythropoiesis due to intrauterine hypoxia.
    - **Complications:** Viscosity-related problems, jaundice.
6. **Congenital Anomalies:**
    - **Risk:** Increased risk of congenital heart defects, neural tube defects, and caudal regression syndrome.
    - **Mechanism:** Hyperglycemia-induced teratogenic effects during organogenesis.
7. **Hypocalcemia and Hypomagnesemia:**
    - **Pathophysiology:** Possibly related to diabetogenic effects on parathyroid function and renal magnesium handling.

Management of IDMs:

1. **Antenatal Care:**
    - **Maternal Glycemic Control:** Tight control of maternal blood glucose levels is crucial.
    - **Fetal Surveillance:** Regular monitoring for fetal growth and well-being.
2. **Delivery Planning:**
    - **Timing and Mode:** Consideration of elective delivery for macrosomic fetuses; readiness for potential complications.
3. **Immediate Postnatal Care:**
    - **Blood Glucose Monitoring:** Frequent monitoring of neonatal blood glucose levels.
    - **Management of Hypoglycemia:** Prompt administration of intravenous glucose if necessary.
4. **Respiratory Support:**
    - **Surfactant Therapy:** For infants with RDS.
    - **Mechanical Ventilation:** If required, based on the severity of respiratory distress.
5. **Cardiac Monitoring:**
    - **Echocardiography:** To assess for cardiomyopathy and other cardiac anomalies.
    - **Management of Cardiomyopathy:** May include medical management or, in severe cases, surgical intervention.
6. **Management of Polycythemia and Hyperbilirubinemia:**
    - **Hydration:** Adequate hydration to reduce blood viscosity.
    - **Phototherapy:** For significant jaundice.
7. **Calcium and Magnesium Supplementation:**

- **Monitoring and Supplementation:** As needed based on laboratory findings.

8. **Long-term Follow-up:**
   - **Metabolic Surveillance:** Monitoring for signs of obesity, diabetes, or other metabolic disorders.
   - **Developmental Surveillance:** Given the increased risk of developmental delays.

Issues in IDMs	Clinical Features	Evaluation	Management
Macrosomia	Birth weight >90th percentile Large for gestational age; Head size normal. Increased body fat and muscle mass	Prenatal ultrasound for fetal size Monitoring for signs of birth trauma during delivery	Careful delivery planning to avoid birth trauma Monitoring for hypoglycemia post-delivery
Hypoglycemia	Jitteriness Cyanosis Seizures Apnea Tachypnea Poor feeding	Frequent blood glucose monitoring post-delivery Monitoring for signs of neurological distress	Prompt administration of IV glucose if necessary Feeding support Continuous glucose monitoring
Respiratory Distress Syndrome (RDS)	Tachypnea Grunting Retractions Cyanosis	Chest X-ray Blood gas analysis	Surfactant therapy if indicated Respiratory support, including oxygen or mechanical ventilation
Cardiomyopathy	Cardiac murmur Tachycardia Signs of heart failure	Echocardiography ECG	Medical management of heart failure if present Monitoring for outflow tract obstruction
Polycythemia and Hyperbilirubinemia	Ruddy complexion (polycythemia) Jaundice (hyperbilirubinemia)	Hematocrit for polycythemia Serum bilirubin levels	Hydration for polycythemia Phototherapy for hyperbilirubinemia
Congenital Anomalies	Varies based on the specific anomaly (e.g.,	Prenatal ultrasound	Surgical or medical management depending on the anomaly

	cardiac defects, neural tube defects)	Postnatal physical examination and imaging as indicated	
Hypocalcemia and Hypomagnesemia	Neuromuscular irritability Seizures	Serum calcium and magnesium levels	Calcium and magnesium supplementation as needed
Long-term Metabolic Risks	Risk of obesity Impaired glucose tolerance Type 2 diabetes	Regular pediatric follow-up Monitoring growth parameters and glucose levels	Lifestyle interventions (diet, exercise) Monitoring for early signs of metabolic syndrome

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2.a. Chronic kidney disease management

- Management of CKD requires a comprehensive, patient-centered approach, focusing on early detection, management of underlying causes and complications, and preparation for renal replacement therapy.
- The role of the nephrologist is pivotal in guiding patients through the complexities of CKD management, ensuring optimal outcomes and quality of life

Initial Approach

History and Physical Examination:

- CKD often presents subtly, making a thorough history and physical examination crucial.
- Key aspects include hypertension, diabetes mellitus, abnormal urinalyses, drug history (analgesics, NSAIDs, penicillamine, antimicrobials, chemotherapeutic agents, antiretroviral agents, proton pump inhibitors, phosphate-containing bowel cathartics, lithium, and exposure to medical imaging radiocontrast agents), and family history of kidney disease.
- Physical examination should focus on blood pressure, funduscopy, and signs of target organ damage from hypertension.

Laboratory Investigation

- **Serum and Urine Protein Electrophoresis**: Essential for all patients with unexplained CKD, especially if associated with anemia and elevated or inappropriately normal serum calcium concentration.
- **Autoimmune and Infectious Etiologies**: Assessment for lupus, hepatitis B and C, and HIV in the presence of glomerulonephritis.
- **Renal Function Monitoring**: Serial measurements to determine the pace of renal deterioration.
- **Metabolic Bone Disease Evaluation**: Serum concentrations of calcium, phosphorus, vitamin D, and PTH.
- **Anemia Workup**: Hemoglobin concentration, iron, B12, and folate levels.
- **24-hour Urine Collection**: For protein excretion assessment.

Imaging Studies

- **Renal Ultrasound**: First-line imaging to assess kidney size, rule out masses and obstruction, and evaluate for chronicity.
- **Doppler Sonography, Nuclear Medicine Studies, CT or MRI**: For diagnosing renovascular disease.
- **Voiding Cystogram**: In cases of suspected reflux nephropathy.

Renal Biopsy

- **Indications**: Generally avoided in bilaterally small kidneys due to risks and often unyielding results.
- Considered in early CKD stages (1–3) if there's suspicion of an active process like interstitial nephritis or accelerated GFR loss.

Establishing the Diagnosis and Etiology of CKD

- **Differentiating Acute from Chronic**: Previous serum creatinine measurements are invaluable.
- Evidence of metabolic bone disease, normochromic anemia, and reduced kidney size (<8.5 cm) favor CKD.

- **Clinical Diagnosis**: In cases like diabetic nephropathy with typical features, biopsy may not be necessary. Ischemic nephropathy is usually diagnosed clinically.

Treatment: Chronic Kidney Disease

- **Specific Treatments**: Include optimized glucose control in diabetes, immunomodulatory agents for glomerulonephritis, and therapies for polycystic kidney disease.
- **Sequential GFR Measurement**: To monitor progression and identify superimposed acute processes.

Clinical Action Plan

- **Staging**: Based on GFR, with actions including diagnosis and treatment, treatment of comorbid conditions, slowing progression, CVD risk reduction, evaluating and treating complications, and preparation for kidney replacement therapy.

Stage of CKD	*Description*	GFR, mL/min per 1.73 m^2	Action
1	*Kidney damage with normal or GFR*	90	Diagnosis and treatment, treatment of comorbid conditions, slowing progression, CVD risk reduction
2	*Kidney damage with mild GFR*	60-89	Estimating progression
3	*Moderate GFR*	30-59	Evaluating and treating complications
4	*Severe GFR*	15-29	Preparation for kidney replacement therapy
5	*Kidney failure*	< 15/ on dialysis	RRT - Kidney replacement (if uremia present)

Slowing the Progression of CKD

- **Reducing Intraglomerular Hypertension and Proteinuria**: Control of systemic and glomerular hypertension is crucial.
    - ACE inhibitors and ARBs are first-line for reducing proteinuria.
- **Slowing Progression of Diabetic Renal Disease**: Emphasizes glycemic control and management of hypertension and proteinuria.

- **Protein Restriction**: Recommended, especially in proteinuric and diabetic renal diseases, with monitoring of nutritional status.

Managing Other Complications of Chronic Kidney Disease

- **Medication Dose Adjustment**: Necessary for many drugs, with avoidance of nephrotoxic agents.
- ***Medical Management:***
  - **Blood Pressure Control:** Antihypertensive medications like ACE inhibitors or ARBs are often used to control hypertension, a common comorbidity in CRF. Target BP is generally <130/80 mm Hg or below 95th centile for age and gender.
  - **Glycemic Control:** In diabetic children, strict glycemic control is essential to prevent further renal damage. Insulin or oral hypoglycemic agents may be used. However clinical scenario of Type 1 DM with CRF is less common
- ***Electrolyte and Acid-Base Balance:***
  - Hyperkalemia: Management includes dietary restriction, medications like sodium polystyrene sulfonate, and in severe cases, hemodialysis.
  - Metabolic Acidosis: Sodium bicarbonate supplements can be used to correct acid-base imbalances.
- ***Anemia Management:***
  - Erythropoiesis-Stimulating Agents (ESAs): Drugs like epoetin alfa are used to stimulate red blood cell production.
  - Iron Supplementation: Intravenous or oral iron supplements are often necessary to support erythropoiesis.
- ***Bone and Mineral Metabolism:***
  - Phosphate Binders: Drugs like sevelamer or calcium acetate are used to control hyperphosphatemia.
  - Vitamin D Supplementation: Calcitriol or other vitamin D analogs are used to manage secondary hyperparathyroidism.
- ***Fluid and Volume Management:***
  - Diuretics: Loop diuretics like furosemide are commonly used to manage fluid overload.

- Sodium Restriction: Dietary sodium restriction is advised to control hypertension and edema.

- ***Nutritional Support:***
  - Protein Restriction: A low-protein diet may be recommended to reduce the workload on the kidneys.
  - Caloric Intake: Adequate caloric intake is essential to prevent malnutrition, a common issue in CRF.
- ***Dialysis:***
  - **Hemodialysis**: Involves the use of a machine to filter waste products from the blood. Typically done 3 times a week.
  - **Peritoneal Dialysis**: Uses the patient's peritoneum as a natural filter. CAPD - Can be done at home but requires frequent exchanges.
- ***Renal Transplantation:***
  - Pre-Transplant Evaluation: Comprehensive assessment to determine suitability for transplantation.
  - Immunosuppressive Therapy: Post-transplant medications like tacrolimus or cyclosporine are essential to prevent graft rejection.
- ***Palliative and Supportive Care:***
  - Pain Management: Opioids or non-opioid analgesics may be used for pain control.
  - Psychological Support: Counseling and support groups can help manage the emotional burden of CRF.
- ***Monitoring and Follow-up:***
  - Regular Lab Tests: Monitoring of renal function, electrolytes, and other parameters is essential for timely intervention.
  - Imaging: Renal ultrasounds or other imaging modalities may be used for ongoing assessment.
- ***Patient Education:***
  - Lifestyle Modifications: Lifestyle Modifications: Focus on creating a child-friendly environment that encourages adherence to treatment.
  - Medication Adherence: Parents are educated on the importance of medication timing and dosing for their children.

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2.b. Amniocentesis

- Amniocentesis remains a valuable tool in prenatal diagnosis, providing critical information that can inform management decisions during pregnancy
- It should be offered with comprehensive genetic counseling to ensure that expectant parents are fully informed and supported throughout the process.
- Amniocentesis is a prenatal diagnostic procedure that involves the extraction of a small amount of amniotic fluid from the amniotic sac surrounding a developing fetus
- This fluid contains fetal cells and various chemicals produced by the baby, which can provide valuable information about the baby's health

Indications for Amniocentesis:

- **Genetic Testing:**
  - To detect chromosomal abnormalities such as Down syndrome (trisomy 21), Edwards syndrome (trisomy 18), or Patau syndrome (trisomy 13).
  - To diagnose genetic disorders like cystic fibrosis or sickle cell disease if there is a known family history or carrier status.
- **Neural Tube Defects:**
  - To assess the level of alpha-fetoprotein (AFP) which can be elevated in cases of spina bifida or anencephaly.
- **Fetal Infections:**
  - To diagnose intrauterine infections such as rubella, cytomegalovirus, or toxoplasmosis.
- **Fetal Lung Maturity:**
  - In cases where early delivery is being considered, to evaluate the maturity of the baby's lungs by measuring levels of phospholipids.
- **Rh Disease:**
  - To determine the severity of hemolytic disease in the fetus due to Rh incompatibility.

Procedure:

- **Ultrasound Guidance:**

- An ultrasound is performed before and during the procedure to locate the placenta, fetus, and pockets of amniotic fluid.

- **Needle Insertion:**
  - A long, thin needle is inserted through the mother's abdominal wall, then the uterus, and into the amniotic sac, avoiding the fetus and umbilical cord.
- **Fluid Withdrawal:**
  - Around 15-20 milliliters of amniotic fluid is withdrawn for analysis.
- **Post-procedure Monitoring:**
  - The fetal heart rate is monitored to ensure the fetus has tolerated the procedure well.

Risks and Complications:

- **Miscarriage:**
  - The risk of miscarriage is approximately 0.1 to 0.3 percent, which is slightly higher than the risk in a pregnancy without amniocentesis.
- **Leakage of Amniotic Fluid:**
  - There may be a small risk of amniotic fluid leakage from the needle puncture site.
- **Infection:**
  - There is a low risk of introducing an infection into the uterus.
- **Rh Sensitization:**
  - Rh-negative mothers may develop antibodies against the fetus's blood cells if they are Rh-positive; Rh immunoglobulin can prevent this.

Timing:

- Typically performed between the 15th and 20th weeks of gestation, although it can be done later in pregnancy if needed.

Results:

- **Genetic Results:**
  - Karyotyping can take several weeks, while rapid results from techniques like FISH or PCR can be available within a few days.
- **Accuracy:**

- Amniocentesis is more than 99% accurate in diagnosing chromosomal abnormalities.

Alternatives:

- **Non-invasive Prenatal Testing (NIPT):**
  - A blood test that can screen for certain genetic conditions with no risk to the fetus.
- **Chorionic Villus Sampling (CVS):**
  - An alternative invasive test that can be performed earlier in the pregnancy but carries a slightly higher risk of miscarriage.

Ethical Considerations:

- **Informed Consent:**
  - Parents must be fully informed about the risks, benefits, and potential outcomes of the test.
- **Decision Making:**
  - Parents may face difficult decisions if a serious abnormality is detected.

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3.a. Neonatal thrombocytopenia

- Neonatal thrombocytopenia, a condition characterized by a platelet count of less than 150,000/µL in a newborn, is a common hematologic disorder in neonates.
- It's essential to categorize the causes based on the timing of onset (early vs. late) and the clinical status of the infant (sick vs. well) for accurate diagnosis and management.

Early-Onset Thrombocytopenia (within the first 72 hours of life)

In Sick Neonates

- **Placental Insufficiency**: Resulting from conditions like preeclampsia or intrauterine growth restriction (IUGR).
- **Perinatal Asphyxia**: Hypoxia during birth can lead to thrombocytopenia.
- **Infection**: Early-onset sepsis, particularly bacterial infections.
- **Polycythemia**: High hematocrit levels can be associated with thrombocytopenia.
- **Congenital Infections**: TORCH infections (Toxoplasmosis, Other agents, Rubella, Cytomegalovirus, and Herpes simplex virus).

In Well Neonates

- **Neonatal Alloimmune Thrombocytopenia (NAIT)**: Caused by maternal antibodies against fetal platelet antigens, most commonly human platelet antigen-1a (HPA-1a).
- **Maternal Immune Thrombocytopenia (ITP)**: Maternal antibodies against platelets cross the placenta.
- **Genetic Syndromes**: Such as trisomy 13, 18, or 21, which can present with thrombocytopenia.
- **Congenital Bone Marrow Failure Syndromes**: Rare but important to consider.

Late-Onset Thrombocytopenia (after 72 hours of life)

In Sick Neonates

- **Nosocomial Infections**: Late-onset sepsis, often due to hospital-acquired organisms.
- **Necrotizing Enterocolitis (NEC)**: Particularly in preterm infants.
- **Chronic Lung Disease**: Especially in preterm infants requiring prolonged respiratory support.
- **Drug-Induced**: Certain medications used in neonatal care can cause thrombocytopenia.
- **Post-Transfusion Purpura**: Rare, following blood product transfusions.

In Well Neonates

- **Late-Onset Neonatal Alloimmune Thrombocytopenia**: Less common than early-onset but still possible.
- **Autoimmune Thrombocytopenia**: Can occur in infants of mothers with autoimmune disorders.
- **Kasabach-Merritt Phenomenon**: Associated with vascular tumors like hemangiomas.
- **Post-Viral Infection**: Viral infections leading to immune-mediated platelet destruction.

Diagnostic Approach

- **Clinical History**: Maternal history of thrombocytopenia, medications, infections.
- **Physical Examination**: Look for signs of bleeding or petechiae.
- **Laboratory Tests**: Complete blood count, blood smear, maternal and neonatal platelet antigen typing in suspected NAIT.
- **Bone Marrow Examination**: If bone marrow failure syndromes are suspected.

Management

- **General Approach**: Depends on the underlying cause, severity of thrombocytopenia, and clinical symptoms.
- **Immunoglobulins**: In cases of immune-mediated thrombocytopenia.
- **Management of Underlying Condition**: Treating infections, managing NEC, adjusting medications.
- **Platelet Transfusions**: Reserved for severe thrombocytopenia or active bleeding.

Indications for platelet transfusion:

Clinical Scenario	Platelet Count Threshold for Transfusion	Indications/Notes
Active Bleeding	<50,000/µL	Immediate transfusion is often necessary to control bleeding.
Major Surgery or Invasive Procedure	<50,000/µL	Prophylactic transfusion to prevent perioperative bleeding.
Central Nervous System (CNS) Bleeding or Surgery	<100,000/µL	Higher threshold due to the risk of intracranial hemorrhage.
Extremely Low Birth Weight (ELBW) Infants	<30,000/µL	Prophylactic transfusion in asymptomatic ELBW infants due to high risk of intracranial hemorrhage.
Stable, Non-Bleeding >1.5kg Neonates	<20,000/µL	Threshold for prophylactic transfusion in stable neonates without active bleeding.
Platelet Dysfunction	<100,000/µL	In cases of qualitative platelet defects, higher thresholds may be necessary.
Neonatal Alloimmune Thrombocytopenia (NAIT)	<30,000/µL or higher based on severity	Transfusion may be needed even at higher counts due to the risk of intracranial hemorrhage.
Exchange Transfusion	<50,000/µL	Prior to exchange transfusion in neonates with severe anemia or hyperbilirubinemia.
Sepsis or NEC	<50,000/µL	In neonates with sepsis or necrotizing enterocolitis, a higher threshold is often used.

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3.b. Haemophilia A management

- Management of Hemophilia A, a genetic disorder characterized by deficient or defective factor VIII, requires a comprehensive approach that includes both preventive and therapeutic strategies
- The management of Hemophilia A is multifaceted, involving regular factor VIII replacement, management of bleeding episodes, inhibitor monitoring, and supportive care
- Advances in treatment, including gene therapy, hold promise for improved outcomes
- Patient education and a multidisciplinary approach are key to effective management and improving the quality of life for individuals with Hemophilia

Prophylactic Treatment

- **Factor VIII Concentrates**: Regular infusions to maintain factor VIII levels and prevent bleeding episodes.
- **Primary Prophylaxis**: Initiated in young children, often before age 3, to prevent joint damage.
- **Secondary Prophylaxis**: Started after the first significant bleeding episode or joint damage.

On-Demand Treatment

- **Factor VIII Replacement**: Administered during bleeding episodes to control and prevent further bleeding.
- **Dosing**: Based on the severity of bleeding and individual pharmacokinetics of factor VIII.

Management of Bleeding Episodes

- **Early Treatment**: Prompt administration of factor VIII at the first sign of bleeding.
- **Target Joints**: Special attention to joints with recurrent bleeds, using aggressive factor VIII replacement.
- **Adjunctive Therapies**: Analgesics for pain, physical therapy to maintain mobility.

Inhibitor Development

- **Risk**: Approximately 30% of severe Hemophilia A patients develop inhibitors against factor VIII.
- **Management**: Immune tolerance induction therapy to eliminate inhibitors.
- **Bypassing Agents**: Used when inhibitors are present, such as recombinant factor VIIa or activated prothrombin complex concentrate.

Surgical Management

- **Preoperative Planning**: Factor VIII levels should be normalized before any surgical procedure.
- **Postoperative Care**: Continued factor VIII replacement to maintain adequate levels during the healing period.

Gene Therapy

- **Emerging Treatments**: Research is ongoing in gene therapy to provide a long-term cure by correcting the underlying genetic defect.

Supportive Care

- **Physical Therapy**: To maintain muscle strength and joint health.
- **Pain Management**: Non-steroidal anti-inflammatory drugs (NSAIDs) should be used cautiously; acetaminophen is preferred.
- **Vaccination**: Hepatitis A and B vaccines are recommended due to the risk of blood-borne infections.

Patient Education and Lifestyle Modifications

- **Avoidance of Trauma**: Engaging in safe physical activities to minimize the risk of bleeding.
- **Self-Infusion Training**: For patients and families, to manage prophylaxis and treatment at home.
- **Regular Monitoring**: Regular check-ups with a hematologist and monitoring of factor VIII levels.

Psychosocial Support

- **Counseling**: For patients and families to cope with the psychological impact of the disease.
- **Education**: About the disease, its management, and prevention of complications.

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4.a. Transport of critically ill newborn

Transporting a sick newborn, especially one that is critically ill, requires meticulous planning, specialized equipment, and a skilled transport team to ensure the infant's stability and safety.

Pre-transport Coordination:

- Thorough communication between the referring and receiving hospitals to understand the infant's condition and transport needs.

- A detailed transport plan, including the route, mode of transport, and estimated time of arrival.

2. **Transport Team Composition**:
    - A multidisciplinary team typically includes a neonatologist or pediatrician, a neonatal nurse, and a respiratory therapist.
    - Team members should have specialized training in neonatal transport and emergency care.
3. **Equipment and Supplies**:
    - A transport incubator that provides a controlled thermal environment.
    - Portable monitors for continuous assessment of vital signs, including heart rate, respiratory rate, oxygen saturation, and blood pressure.
    - Emergency medications and supplies, intubation equipment, and intravenous fluids.
    - Portable ventilators and oxygen supply for respiratory support.
4. **Medical Management During Transport**:
    - Ensuring adequate ventilation and oxygenation throughout the transport.
    - Maintenance of normothermia to prevent cold stress or hyperthermia.
    - Secure vascular access for medication administration and fluid resuscitation.
    - Continuous monitoring and support of blood glucose levels and electrolyte balance.
5. **Stabilization Prior to Transport**:
    - The newborn should be hemodynamically stable before transport.
    - Necessary interventions, such as surfactant administration for respiratory distress syndrome, should be performed at the referring hospital.

Clinical Scenario	**Medical Management During Transport**
Respiratory Distress	Oxygen therapy to maintain SpO2 within target range. Mechanical ventilation if indicated, with settings adjusted to maintain adequate ventilation and minimize barotrauma.

	Surfactant therapy prior to transport if indicated and not already administered. Continuous monitoring of respiratory status and gas exchange.
Cardiovascular Instability	Inotropic support (e.g., dopamine, dobutamine) to maintain blood pressure and perfusion. PGE1 to be started before starting transport and neonate to be intubated in anticipation of apneas (side effect of PGE1) . Volume resuscitation with isotonic fluids or blood products if indicated. Echocardiography prior to transport if available to assess cardiac function. Monitoring for arrhythmias and treating as necessary.
Suspected Sepsis	Broad-spectrum antibiotics administered after obtaining cultures. Fluid resuscitation and vasopressor support if signs of shock are present. Monitoring for signs of worsening condition or organ dysfunction. Thermoregulation to prevent hypothermia.
Neurological Concerns (e.g., Seizures)	Anticonvulsants to manage seizure activity. Sedation as needed to prevent agitation and further neurological insult. Head positioning to avoid increased intracranial pressure. Monitoring for changes in neurological status.
Gastrointestinal Complications (e.g., NEC)	Gastric decompression with an orogastric or nasogastric tube. Discontinuation of enteral feeds. Administration of antibiotics if NEC is suspected. Close monitoring for abdominal distension and signs of perforation.
Hypoglycemia	Intravenous dextrose to correct low blood sugar levels. Frequent monitoring of blood glucose. Adjustment of dextrose infusion rate based on glucose readings. Consideration of underlying causes such as hyperinsulinism.
Thermal Instability	Use of a transport incubator to maintain a neutral thermal environment. Monitoring of core temperature.

	Warm IV fluids and warm humidified respiratory gases if needed. Avoidance of excessive handling to minimize heat loss.
Jaundice	Phototherapy during transport if bilirubin levels are high. Monitoring bilirubin levels if possible. Ensuring adequate hydration to promote bilirubin excretion.
Hemodynamic Monitoring	Use of umbilical or peripheral arterial catheter for continuous blood pressure monitoring. Central venous pressure monitoring if central access is available. Frequent assessment of capillary refill, heart rate, and blood pressure.
Pain and Stress	Administration of analgesics or sedatives as appropriate. Non-pharmacological interventions such as swaddling or pacifiers. Minimizing stimuli (e.g., noise, light) during transport.

6. **Communication**:
    - Open lines of communication between the transport team, referring clinicians, and the receiving facility.
    - Regular updates should be provided to the parents or guardians about the infant's status.
7. **Safety Measures**:
    - Adherence to strict protocols for infection control.
    - Securement of the infant and all equipment to prevent dislodgement during transport.
    - Regular checks on equipment functionality and battery life.
8. **Documentation**:
    - Detailed records of the infant's condition, interventions prior to and during transport, and vital signs monitoring.
    - Transfer of all pertinent medical records to the receiving facility.
9. **Training and Simulation**:
    - Regular training exercises and simulations for the transport team to maintain proficiency in emergency scenarios.

- Drills to practice the setup and use of transport equipment.

10. **Modes of Transport**:
    - Selection of transport mode (ground ambulance, helicopter, fixed-wing aircraft) based on distance, weather, and the infant's condition.
    - Consideration of the risks associated with each mode, such as vibration and noise in air transport.
11. **Ethical Considerations**:
    - Decisions about transport should consider the potential benefits and risks to the infant.
    - Respect for the family's needs and wishes, ensuring they are informed and supported throughout the process.
12. **Quality Improvement**:
    - Post-transport debriefings to identify any issues and opportunities for improvement.
    - Data collection and analysis for quality improvement initiatives.
13. **Legal and Regulatory Compliance**:
    - Compliance with regional and national regulations governing neonatal transport.
    - Ensuring all team members are credentialed and certified as required.
14. **Parental Support and Communication**:
    - Providing emotional support and clear information to the parents about their infant's condition, the transport process, and what to expect.
    - Arranging for the parents to be with their infant as soon as possible after arrival at the receiving facility.
15. **Follow-up and Continuity of Care**:
    - Ensuring a smooth handover to the receiving team, with a comprehensive briefing on the care provided during transport.
    - Follow-up to assess the outcomes of the transport and the infant's subsequent progress.

Issues related to transport of sick newborn

Issue	Description	Management Strategies
Thermal Regulation	Newborns are at risk of hypo- or hyperthermia due to immature thermoregulation.	Use of transport incubators, warm blankets, and continuous temperature monitoring.
Respiratory Management	Immature lungs may require support such as oxygen, CPAP, or mechanical ventilation.	Appropriate respiratory support equipment and monitoring; adjustments for altitude changes during air transport.
Cardiovascular Stability	Fluctuating blood pressure and the need for fluid management or inotropic support.	Continuous cardiovascular monitoring and securement of lines and equipment.
Infection Control	Increased risk of infection due to invasive procedures and exposure to different environments.	Adherence to strict aseptic technique and infection control protocols.
Vibration and Noise	Transport can subject infants to stress and potential harm from vibration and noise.	Use of sound-attenuating incubators and vibration-dampening equipment.
Equipment and Power Failures	Reliability of transport equipment and power is crucial for patient safety.	Regular equipment checks, backup systems, and ensuring sufficient battery life.
Communication Challenges	Effective communication is critical but can be hampered by environmental factors.	Clear communication protocols and backup methods for potential system failures.
Limited Access to Emergency Interventions	Limited resources for unexpected emergencies during transport.	Transport team preparedness and self-sufficiency to manage emergencies.
Parental Concerns and Separation	Parental anxiety about the transport process and separation from their infant.	Providing information, emotional support, and facilitating contact if possible.
Legal and Ethical Issues	Consent and ethical decisions about the extent of care during transport.	Obtaining informed consent and considering ethical implications of transport decisions.

Training and Competency	The need for specialized training in neonatal transport medicine.	Regular education, simulation training, and competency assessments for the transport team.
Cost and Resource Utilization	Transport can be expensive and resource-intensive.	Efficient resource use and cost-effective strategies for sustainable transport programs.
Environmental Factors	Weather and traffic conditions can impact transport safety and timing.	Planning for environmental contingencies and choosing appropriate transport modes.
Documentation and Data Collection	Need for accurate documentation and data for continuity of care and quality improvement.	Thorough documentation during transport and systematic data collection for analysis.
Quality Improvement	Continuous improvement is necessary to enhance transport safety and outcomes.	Regular case reviews, outcome analysis, and implementation of improvement initiatives.

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4.b. Therapeutic hypothermia

Mechanisms of action:

1. ***Reduction of Metabolic Demand:***
    - Cooling reduces the metabolic rate of brain tissue, decreasing the demand for oxygen and glucose.
    - This reduction in metabolic demand helps to preserve energy stores and mitigate the extent of brain injury caused by hypoxia and ischemia.
2. ***Inhibition of Excitotoxicity:***
    - Hypothermia inhibits the release of excitatory neurotransmitters like glutamate.
    - This inhibition reduces excitotoxicity, a process where excessive stimulation by neurotransmitters leads to neuronal damage and death.

3. ***Attenuation of Cerebral Edema:***
    - Cooling reduces cerebral edema (swelling of the brain), which is a common consequence of hypoxic-ischemic injury.
    - By decreasing edema, hypothermia helps to maintain cerebral blood flow and reduce intracranial pressure.
4. ***Reduction of Inflammatory Response:***
    - Hypothermia modulates the inflammatory response in the brain, reducing the production of pro-inflammatory cytokines.
    - This modulation helps to prevent further damage from inflammation following reperfusion (restoration of blood flow).
5. ***Preservation of the Blood-Brain Barrier:***
    - Cooling helps to maintain the integrity of the blood-brain barrier, which is often compromised in HIE.
    - This preservation prevents the influx of potentially harmful substances into the brain tissue.
6. ***Reduction of Apoptosis (Programmed Cell Death):***
    - Hypothermia inhibits apoptotic pathways activated by hypoxic-ischemic injury.
    - This reduction in apoptosis helps to preserve viable brain tissue.
7. ***Decreased Production of Free Radicals:***
    - Cooling reduces the generation of harmful free radicals and reactive oxygen species that are typically produced in large quantities during and after ischemic events.
    - This decrease helps to minimize oxidative stress and subsequent cellular damage.
8. ***Modulation of Cellular Repair Mechanisms:***
    - Hypothermia may influence various cellular repair processes, promoting the recovery of neurons and glial cells after injury.
9. ***Long-Term Neuroprotection:***
    - The benefits of therapeutic hypothermia extend beyond the immediate treatment period, offering long-term neuroprotection.

- Studies have shown improved neurological outcomes in infants treated with hypothermia compared to those who received standard care.

Clinical Application:

- **Timing and Duration:** Therapeutic hypothermia is typically initiated within 6 hours of birth and continued for 72 hours.
- **Target Temperature:** The target body temperature is usually maintained between 33.5°C and 34.5°C.
- **Monitoring:** Continuous monitoring of core body temperature, heart rate, blood pressure, and oxygenation is essential.
- **Post-Therapy Care:** Gradual rewarming and careful monitoring for any complications are crucial after the hypothermia treatment period.

- **Indication**: Indicated for infants with moderate to severe HIE if initiated within 6 hours of birth.
- **Method**: The infant's core body temperature is reduced to 33-34°C for 72 hours using a cooling blanket – **whole body cooling**.

Who is eligible for hypothermia?

To undergo therapeutic hypothermia, a neonate should be ≥36 weeks and ≥1800 grams and should satisfy point **a & b** (stated below)

(a). At least one of the Following:

- Apgar score of ≤ 5 at 10 min after birth
- Continued need for Resuscitation (IPPV) at 10 min after birth
- Acidosis within 60 min of birth (Defined as any occurrence of umbilical cord or Arterial or Capillary pH < 7.00)
- Base deficit ≥ 16 mmol/L in umbilical cord or any blood sample within1 hour of birth (arterial, venous or capillary)

Infants that meet criteria (a) should be assessed for whether they meet the neurological abnormality criteria (b)

(b) Seizures (or) moderate to severe encephalopathy

Moderate to severe encephalopathy consists of (all are required to be present):

- Altered state of consciousness (reduced or absent response to stimulation)

- Abnormal tone (focal or general hypotonia, or flaccid)
- Abnormal primitive reflexes (weak or absent suck or Moro response)

Note:

- Seizures detected by EEG or aEEG without a clinical component (subclinical seizures) would also be considered as seizures
- In babies who satisfy criteria (a) & (b), start therapeutic hypothermia at the earliest, but not later than 6 hours
- Examine and record a baseline (pre-TH) encephalopathy severity score (Thompson's score – Given at Section G in this chapter)

Who should not undergo Therapeutic Hypothermia:

- Gestational age <36 weeks (confirmed by reliable LMP or early antenatal ultrasound or New Ballard scoring system – in this order of importance) (currently this is getting flexible with upcoming trials)
- Birth weight <1800 grams
- Postnatal age greater than 6 hours
- Presence of known chromosomal anomalies
- Presence of major congenital malformations
- Active bleeding (Bleeding from > 2 sites)
- Grade 3 and above Intracranial hemorrhage (Therapeutic hypothermia not to be delayed if USG has not been done, but USG head to be done within 24 hours of birth and a decision regarding discontinuation of hypothermia has to be taken in Gr III IVH / Intra-Parenchymal Bleed)
- Moribund neonate

- **Mechanism**: Hypothermia is believed to reduce metabolic demand, inhibit harmful biochemical cascades, and reduce cerebral edema.
- **Monitoring During Hypothermia**: Continuous monitoring of core temperature, heart rate, blood pressure, oxygen saturation, and blood glucose levels is essential. Electroencephalography (EEG) may be used to monitor for seizures.
- **Rewarming**: After 72 hours, the infant is slowly rewarmed to a normal body temperature at a controlled rate to prevent rebound cerebral edema or other complications.

Seizure Management:

- **Detection**: Seizures in neonates may be subtle; hence, continuous EEG monitoring is often used in infants with HIE.
- **Treatment**: Anticonvulsants such as phenobarbital or levetiracetam are used to control seizures. The choice of medication is based on seizure type, efficacy, and side-effect profile. Topiramate is promising due to its neuroprotective effects

Monitoring of a neonate in TH:

Parameter	Frequency
Vital parameters	HR (Anticipate severe Bradycardia), respiratory rate, blood pressure and oxygen saturation – continuous and document every 1 hour
Thompson score	Every 6 hours
Blood sugar	Every 6 hours or earlier if indicated
Complete blood counts including platelet counts	Baseline Every 24 h thereafter till completion of therapy
Blood urea, Serum Creatinine	Baseline Every 24 h thereafter till completion of therapy
Coagulation profile	Baseline Every 24 h thereafter till completion of therapy
Serum electrolytes	Sodium and Potassium – Baseline and every 12 hours Calcium – baseline and later wherever indicated
Blood gas	As indicated due to ventilatory requirements
Sepsis work-up	CRP and any other acute phase reactant – Baseline and as indicated. Blood culture – at the start of antibiotics
Liver function tests (SGOT and SGPT)	Baseline At end of therapy
USG head	Baseline within 24 hrs of starting hypothermia or earlier if there is clinical bleeding. at 48 h and completion of therapy
Amplitude-integrated EEG (aEEG)	Continuous while on hypothermia
MRI brain	Between 7th and 14th day of birth

Neuroprotective Strategies:

- **Pharmacological Interventions**: Research is ongoing into drugs that can provide neuroprotection, such as topiramate, erythropoietin and allopurinol, but these are not yet standard treatments.
- **Optimization of Cerebral Oxygenation**: Careful management of ventilation to avoid hypoxia or hyperoxia, both of which can be damaging to the injured brain.

Nutritional Support:

- **Feeding**: Enteral feeding may be delayed or contraindicated in the acute phase. Parenteral nutrition is provided until enteral feeds can be safely initiated.
- **Glucose Management**: Maintaining normoglycemia is important as both hypoglycemia and hyperglycemia can worsen outcomes.

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5.a. Apnea of prematurity

Apnea of prematurity (AOP) is a common condition affecting preterm infants, particularly those born before 34 weeks of gestation. It's a diagnosis of exclusion once major causes like infective and metabolic are ruled out.

AAP definition: Apnea is characterized by a cessation of breathing that lasts for more than 20 seconds, or lesser when accompanied by bradycardia and/or oxygen desaturation.

Pathophysiology:

- **Immature Respiratory Control:** In preterm infants, the respiratory control centers in the brain are not fully developed. This immaturity leads to irregular breathing patterns and apnea.
- **Underdeveloped Chemoreceptor Response:** Preterm infants have a blunted response to changes in carbon dioxide and oxygen levels, contributing to the risk of apnea.
- **Weak Respiratory Muscles:** The muscles involved in breathing may not be fully developed in preterm infants, making sustained respiratory effort more challenging.

- **Fetal Respiratory Movements**: These movements are crucial for lung development and are predominantly observed during REM sleep in the third trimester.

- **Medulla Oblongata**: This brainstem region contains centers controlling involuntary functions, crucial for respiratory and cardiovascular regulation.
- **Respiratory Rhythm Generation**: Involves excitatory neurons in the Pre-Bötzinger complex, with impulses routed to respiratory muscles.
- **Developmental Disorder**: AOP results from the physiological immaturity of the respiratory control system in premature infants, exacerbated by neonatal diseases.
- **Ventilatory Responses**: Altered responses to hypoxia and hypercapnia, with a decreased response to $PaCO_2$ in premature infants.
- **Thermoregulation**: Hyperthermia increases apnea risk, suggesting a link between apnea, metabolic state, and environmental temperature.

Clinical Features:

- **Recurrent Apneas:** Episodes of breathing cessation lasting more than 20 seconds.
- **Bradycardia:** Often accompanies apnea episodes, as the heart rate decreases.
- **Oxygen Desaturation:** Reduced oxygen levels in the blood during apnea episodes.
- **Color Changes:** Infants may exhibit pallor or cyanosis during an apneic episode.

Diagnosis:

- **Clinical Observation:** Diagnosis is primarily based on the observation of apneic episodes.
- **Monitoring:** Continuous cardiorespiratory monitoring is essential in preterm infants to detect apnea, bradycardia, and desaturation.
- **Exclusion of Other Causes:** It's important to rule out other causes of apnea such as infection, neurological disorders, metabolic imbalances, and respiratory problems.

Management:

- **General Measures:**
  - **Stimulation:** Gentle tactile stimulation during an apneic episode can prompt the resumption of breathing.
  - **Optimal Thermal Environment:** Maintaining a stable body temperature to reduce metabolic demand.
  - **Adequate Nutrition:** Ensuring proper nutrition to support respiratory muscle function and overall health.
- **Medical Interventions:**

- **Caffeine Citrate:** A central respiratory stimulant that reduces the frequency and severity of apneic episodes. Loading 20mg/kg followed by maintenance of 10mg/kg/day IV/ oral.

Caffeine and AOP

- **Caffeine's Role**: It reduces the occurrence of bronchopulmonary dysplasia and is preferred over theophylline and aminophylline due to lower toxicity risk.
- **Clinical Trials**: Show caffeine's effectiveness in reducing apneic episodes, aiding in extubation, and lowering the risk of neurodevelopmental disorders.

  - **Continuous Positive Airway Pressure (CPAP):** Provides mild air pressure to keep the airways open.
  - **Mechanical Ventilation:** In severe cases, or when CPAP is insufficient.
- **Monitoring and Follow-Up:**
  - **Cardiorespiratory Monitoring:** Continuous monitoring to detect and manage apneic episodes.
  - **Regular Follow-Up:** Monitoring for long-term respiratory and neurological outcomes.

Prognosis:

- **Self-Resolving:** AOP typically resolves as the infant matures, usually by the time they reach the term equivalent age.
- **Long-Term Outcomes:** Most infants with AOP do not have long-term complications, but they should be monitored for potential developmental delays or other issues.

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5.b. Prevention of BPD

This is a challenging approach that involves prenatal, perinatal, and postnatal strategies.

Prenatal Strategies

- **Antenatal Steroids**: Administered to mothers at risk of preterm delivery to accelerate fetal lung maturation and reduce the incidence and severity of respiratory distress syndrome (RDS), a precursor to BPD.
- **Optimal Timing of Delivery**: Avoiding unnecessary early delivery and ensuring that preterm birth is medically indicated to minimize the duration of exposure to potential postnatal lung injuries.

Perinatal Strategies

- **Resuscitation with Room Air**: Using room air instead of 100% oxygen to initiate resuscitation in preterm infants to reduce oxidative stress.
- **Delayed Cord Clamping**: Waiting for 30-60 seconds before clamping the umbilical cord can improve hemodynamic stability and reduce the need for blood transfusions, which are associated with BPD.
- **Gentle Ventilation**: Using less invasive ventilation techniques such as continuous positive airway pressure (CPAP) or nasal intermittent positive pressure ventilation (NIPPV) to minimize barotrauma and volutrauma.
- **Surfactant Administration**: Early (prophylactic) or selective surfactant administration via less invasive methods to reduce the need for mechanical ventilation.

Postnatal Strategies

a) **Avoidance of Mechanical Ventilation**: When possible, using non-invasive respiratory support to reduce lung injury associated with mechanical ventilation with gentle ventilation strategies like VC/VG.

b) **Optimal Oxygen Saturation Targeting**: Maintaining oxygen saturation in a target range that minimizes both hypoxia and hyperoxia, which can contribute to BPD.

c) **Nutritional Support**: Ensuring adequate nutrition for growth and development, including the provision of breast milk, which has protective effects against BPD.

d) **Fluid Management**: Careful fluid management to avoid fluid overload, which can worsen lung function and contribute to BPD.

e) **Diuretics**: Judicious use of diuretics to manage fluid overload and pulmonary edema in established BPD.

f) **Caffeine Therapy**: Used to treat or prevent apnea of prematurity, caffeine has also been shown to reduce the incidence of BPD.

g) **Vitamin A Supplementation**: Has been shown to reduce the risk of BPD in extremely low birth weight infants.

h) **Infection Control**: Rigorous infection control practices to prevent nosocomial infections, which can exacerbate lung injury.

i) **Pharmacological Interventions**: Limited use of postnatal steroids for the prevention of BPD in select cases due to potential adverse effects.

1. **Respiratory Support**:
    - **Non-invasive Ventilation**: Use of CPAP (continuous positive airway pressure) or non-invasive ventilation modes to reduce the need for mechanical ventilation.
    - **Oxygen Therapy**: Supplemental oxygen to maintain adequate oxygenation, with careful monitoring to avoid oxygen toxicity.
    - **Mechanical Ventilation**: In severe cases, mechanical ventilation may be necessary, but the goal is to use the lowest effective pressures and oxygen concentrations.
2. **Nutritional Support**:
    - **Adequate Nutrition**: Ensuring sufficient caloric intake to support growth and lung development.
    - **Specialized Nutrition**: High-calorie diets, and possibly supplements like vitamins A and E, which are important for lung health.
3. **Medications**:
    - **Diuretics**: Used to manage fluid balance and reduce lung congestion.
    - **Bronchodilators**: To improve airway function in some infants.
    - **Corticosteroids**: May be used judiciously to reduce lung inflammation, but they have potential side effects and their use is controversial.
    - **Pulmonary Vasodilators**: In cases with pulmonary hypertension.
4. **Monitoring and Management of Complications**:
    - **Regular Follow-Up**: Monitoring lung function, growth, and development.
    - **Management of Pulmonary Hypertension**: A serious complication of BPD.
    - **Immunizations**: Keeping up with vaccinations, including RSV (respiratory syncytial virus) prophylaxis.
5. **Family Support and Education**:
    - **Parental Education**: On the care of a child with BPD, including nutrition, medication administration, and recognizing signs of respiratory distress.

- **Home Care Preparation**: For infants discharged with oxygen or other supportive therapies.
- **Psychosocial Support**: For families coping with the stress of having a child with a chronic condition.

Long-term Strategies

- **Chronic Care Management**: For infants with established BPD, a chronic care approach including respiratory support, nutritional support, and management of comorbidities.
- **Follow-up and Rehabilitation**: Regular follow-up to monitor lung and neurodevelopmental outcomes and provide interventions as needed.

Research and Future Directions

- **Regenerative Medicine**: Exploring the potential of stem cells and other regenerative therapies to repair lung tissue.
- **Anti-inflammatory Agents**: Investigating new medications to reduce inflammation in the lungs without the side effects of steroids.
- **Genetic and Biomarker Studies**: To better understand the pathogenesis of BPD and identify infants at risk for targeted interventions.

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6.a. Pathophysiology of SAM

- Severe Acute Malnutrition (SAM) is a major health concern, particularly in low- and middle-income countries.
- It represents the most extreme and visible form of undernutrition.
- Its pathophysiology is complex and multifactorial, involving not only inadequate caloric intake but also a host of interrelated factors including infections, environmental conditions, and socio-economic factors.

1. Energy Deficit

- **Caloric Insufficiency**: The primary issue in SAM is an insufficient intake of energy and nutrients. This can be due to a lack of available food, poor dietary quality, or conditions that increase nutritional needs or decrease intake, such as infections or psychological stress.
- **Catabolic State**: The body enters a catabolic state to meet energy demands, leading to the breakdown of body tissues, especially muscle and fat stores.

2. Protein Deficiency

- **Muscle Wasting**: Inadequate protein intake leads to muscle wasting, as the body breaks down muscle proteins to maintain vital functions.
- **Edema**: Hypoalbuminemia, a result of protein deficiency, leads to decreased plasma oncotic pressure and the leakage of fluid into interstitial spaces, causing edema, a hallmark of kwashiorkor, a form of SAM.

3. Micronutrient Deficiencies

- **Vitamins and Minerals**: SAM is often accompanied by deficiencies in essential vitamins and minerals, exacerbating the severity of the condition and complicating recovery.
- **Immune Dysfunction**: Micronutrient deficiencies, particularly of zinc, vitamin A, and selenium, impair immune function, increasing susceptibility to infections.

4. Gastrointestinal Complications

- **Intestinal Atrophy**: Chronic malnutrition leads to atrophy of the intestinal mucosa, reducing nutrient absorption and exacerbating malnutrition.
- **Dysbiosis**: Altered gut microbiota in malnourished individuals can affect nutrient absorption and immune function.
- **Diarrhea**: Frequent in SAM, further impairs nutrient absorption and leads to dehydration and electrolyte imbalances.

5. Metabolic Abnormalities

- **Hypoglycemia**: Due to depleted glycogen stores and impaired gluconeogenesis.
- **Hypothermia**: Reduced metabolic rate and loss of subcutaneous fat lead to difficulty in maintaining body temperature.
- **Electrolyte Imbalances**: Particularly hypokalemia and hypophosphatemia, which can be life-threatening.

6. Infections

- **Increased Susceptibility**: Malnutrition impairs the immune response, making children with SAM more susceptible to infections.
- **Infection-Malnutrition Cycle**: Infections exacerbate malnutrition by increasing metabolic demands and reducing appetite, creating a vicious cycle.

7. Psychosocial and Developmental Impact

- **Cognitive Impairment**: Chronic malnutrition can lead to long-term cognitive and developmental impairments.
- **Psychosocial Deprivation**: Often associated with inadequate social interaction and stimulation, contributing to developmental delays.

8. Systemic Effects

- **Cardiac Function**: Reduced cardiac muscle mass and impaired cardiac function.
- **Anemia**: Common due to a combination of dietary micronutrient deficiencies, chronic inflammation, and infections.

Theories of SAM pathophysiology:

- ❖ The pathophysiology of SAM is a complex interplay of nutritional, immunological, gastrointestinal, metabolic, and psychosocial factors. To elucidate many theories have been proposed
- ❖ These theories highlight the complexity of SAM, indicating that it is a multifactorial condition influenced by dietary intake, metabolic changes, immune response, and socio-economic factors.

Theory/Model	Proponent(s)	Key Concepts and Descriptions
Gopalan's Theory	C. Gopalan	Proposes that protein deficiency is secondary to calorie deficiency. Emphasizes the role of inadequate energy intake leading to the breakdown of body tissues for energy, subsequently causing protein deficiency. Suggests that the primary issue is the lack of sufficient calories rather than protein.
Protein Deficiency Theory	Ancel Keys and others	Initially, it was believed that protein deficiency was the primary cause of malnutrition. This theory led to the distinction between kwashiorkor (protein malnutrition) and marasmus (caloric malnutrition). It focuses on the lack of dietary protein as the central issue in the development of SAM.
Adaptation Theory	J.C. Waterlow	Suggests that malnutrition is an adaptive response to a low nutrient supply. Proposes that the body adapts to undernutrition by reducing growth and metabolic rate to conserve energy. Highlights the body's ability to adjust to prolonged dietary restrictions.
Cytokine Theory	Philip James and others	Focuses on the role of cytokines in malnutrition.

		Suggests that infection and inflammation lead to increased cytokine production, which affects metabolism and can lead to anorexia. Emphasizes the interaction between nutrition, infection, and immune response.
Dual-Deficit Theory	Michael Golden	Proposes that both protein and energy deficiencies are important in the development of SAM. Highlights the role of micronutrient deficiencies in addition to macronutrient deficiencies. Suggests that the combination of multiple nutritional deficits leads to the clinical manifestations of SAM.
Ecological Theory	D.B. Jelliffe	Emphasizes the role of environmental, social, and economic factors in malnutrition. Considers SAM as a result of broader ecological issues including poverty, food scarcity, and lack of healthcare. Focuses on the multifactorial nature of malnutrition beyond just dietary intake.

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6.b. Refeeding syndrome

Definition

- Refeeding syndrome refers to a potentially life-threatening metabolic disturbance that can occur upon reintroduction of nutrition to malnourished or starved individuals.

Pathophysiology

- Characterized by hypophosphatemia, hypokalemia, and hypomagnesemia.
- Shift from catabolism to anabolism, leading to increased cellular uptake of electrolytes.
- Insulin surge promotes cellular uptake of phosphate, potassium, and magnesium.
- Fluid balance alterations, leading to edema and heart failure.

Risk Factors

- Chronic malnutrition, anorexia nervosa, alcoholism.
- Prolonged fasting, starvation, or surgical interventions.

- Severely and chronic malnourished patients, cancer patients, and those with chronic illnesses.

Clinical Manifestations

- Cardiovascular: Tachycardia, hypotension, and, in severe cases, heart failure.
- Neurological: Confusion, seizures, and coma.
- Muscular: Generalized weakness, respiratory failure.
- Hematological: Thrombocytopenia, leukocytosis.

System	Clinical Manifestations
Cardiovascular	Rapid pulse; Increased venous pressure; Hypotension; Decreased stroke volume; Cardiac arrhythmias
Respiratory	Breathlessness; Respiratory failure; Impaired diaphragm contractility; Dyspnea
Neurological	Weakness; Tremor; Tetany; Seizures; Altered mental status; Coma
Gastrointestinal	Rapid enlargement of the liver; Watery diarrhea; Nausea; Vomiting
Hematological	Leukocyte dysfunction; Hemolysis; Thrombocytopenia
Other	Hypophosphatemia; Hypokalemia; Hypomagnesemia

Diagnosis

- Serum electrolytes: Key abnormality: Hypophosphatemia /Low phosphate, Also – low potassium, and magnesium levels.
- ECG changes: Arrhythmias, prolonged QT interval.
- Clinical assessment: History of malnutrition, rapid weight loss, and low BMI.

Management Strategies

- Gradual reintroduction of calories: Start at 10–20 kcal/kg/day, then increase.
- Electrolyte monitoring and repletion: Phosphate, potassium, and magnesium.
- Thiamine supplementation: To prevent Wernicke's encephalopathy.
- Fluid management: Careful fluid resuscitation to prevent fluid overload.

Management Steps	Description

Initial Stabilization	Correct electrolyte imbalances and provide maintenance energy
Controlled Transition	Gradual transition to high-energy feeding
Monitoring	Monitor vital signs and electrolyte levels
Medication	Administer digoxin and furosemide if needed

Complications

- Cardiac arrhythmias, acute heart failure.
- Neurological impairments: Wernicke's encephalopathy, seizures.
- Respiratory failure due to muscle weakness.
- Death, if not promptly and adequately managed.

Prognosis

- Variable, depending on the severity of the syndrome and the effectiveness of management.

Prevention

- Identification of at-risk individuals.
- Gradual reintroduction of nutrition with close monitoring.

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7.a. MR vaccine

- The MR vaccine is a key component of public health strategies to control and eventually eradicate measles and rubella.
- Its widespread use has significantly reduced the incidence of these diseases and their associated complications.
- The MR vaccine is a combination vaccine that protects against two significant viral diseases: Measles and Rubella.

Composition

- **Measles Component**: Live attenuated measles virus, derived from the Edmonston-Zagreb strain.
- **Rubella Component**: Live attenuated rubella virus, derived from the RA 27/3 strain.

Indications

- **Primary Vaccination**: Typically administered to children. The first dose is usually given at 12-15 months of age.
- **Booster Dose**: A second dose is often given at 4-6 years of age, though the schedule can vary depending on the national immunization program.
- **Catch-up Vaccination**: For individuals who missed the vaccine at the recommended age. As a part of MR campaign.

Administration

- **Route**: Subcutaneous injection.
- **Dosage**: Standard dose as per the manufacturer's guidelines.
- **Site**: Commonly administered in the upper arm.

Efficacy and Immunity

- **Measles**: Highly effective in preventing measles, a highly contagious viral disease that can lead to serious health complications.
- **Rubella**: Effective in preventing rubella, which is particularly important for preventing congenital rubella syndrome (CRS) in pregnant women, which can cause serious birth defects.

Safety and Side Effects

- **Common Side Effects**: Fever, mild rash, and swelling or redness at the injection site.
- **Rare Complications**: More serious side effects are rare but can include allergic reactions.

Contraindications

- **Severe Allergic Reactions**: To any component of the vaccine.
- **Immunocompromised Individuals**: Those with weakened immune systems may need to avoid live vaccines.
- **Pregnancy**: Not recommended for pregnant women due to the live virus component.

Public Health Importance

- **Eradication of Measles and Rubella**: The vaccine is crucial in the global efforts to eradicate measles and control rubella, particularly to prevent CRS.
- **Outbreak Control**: Helps in controlling outbreaks of measles and rubella.

MR Campaign

- The MR vaccination campaign in India is a key public health initiative with far-reaching implications for child health and disease eradication.
- Its success hinges on effective implementation, public cooperation, robust surveillance, and sustained efforts to integrate the MR vaccine into routine immunization programs.
- This campaign is a critical step towards achieving the goal of a measles and rubella-free India and contributes significantly to global eradication efforts.
- **Reduction in Disease Burden**: Significant reduction in measles and rubella cases post-campaign.
- **Global Commitment**: Contribution to the global goal of measles and rubella elimination.

Objectives of the MR Campaign

- **Eradication of Measles and Rubella**: To drastically reduce and ultimately eliminate measles and rubella/CRS in India.
- **Immunization Coverage**: To vaccinate a broad segment of the population, particularly children, against these diseases.

Target Population

- **Children Aged 9 Months to 15 Years**: The campaign primarily targets all children in this age group, regardless of their previous vaccination status.
- **Nationwide Reach**: The campaign aims to cover all states and union territories of India.

Implementation Strategy

- **Phased Approach**: The campaign is implemented in phases, targeting different states and regions at different times.

- **School-Based and Community-Based Campaigns**: Vaccinations are administered through schools and community health centers.
- **Integration with Routine Immunization**: Post-campaign, the MR vaccine is intended to replace the measles vaccine in the routine immunization schedule.

MR Vs MMR

- ❖ The decision by the Government of India to focus on the Measles and Rubella (MR) vaccine, rather than the Measles, Mumps, and Rubella (MMR) vaccine, was strategic and based on several considerations specific to India's public health priorities and epidemiology
- ❖ The choice of MR vaccine over MMR by the Government of India reflects a strategic decision based on disease prevalence, public health priorities, resource allocation, and alignment with global health goals
- ❖ While mumps remains a relevant health concern, the immediate focus on measles and rubella addresses the more pressing public health challenges
- ❖ This approach allows for effective utilization of resources, ensuring maximum impact in reducing the burden of these diseases
- ❖ As India progresses in its public health endeavors, the vaccination strategy may evolve in response to changing epidemiological patterns and healthcare objectives.

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7.b. Vitamin B1 deficiency

- ❖ Thiamine (Vitamin B1) deficiency in infants can lead to a range of clinical features, often serious, due to its crucial role in carbohydrate metabolism and neural function
- ❖ Thiamine deficiency in infants is a preventable condition that can have serious consequences if not promptly recognized and treated
- ❖ Awareness of its clinical features and risk factors is crucial for early diagnosis and management, particularly in regions where nutritional deficiencies are common
- ❖ Regular monitoring and dietary guidance can effectively prevent this condition.

Thiamine-responsive megaloblastic anemia (TRMA) syndrome

Autosomal recessive (AR) disorder

Mutations in the SLC19A2 gene, encoding a thiamine transporter protein

- Megaloblastic anemia (MA)
- diabetes mellitus (DM)
- sensorineural hearing loss(SNHL)

Responding in varying degrees to thiamine treatment.

Treatment of TRMA and other dependency states require higher dosages (100-200 mg/day) of thiamine

Biotin and thiamine responsive basal ganglia disease

Results from mutations in the SLC19A3 gene;

Presents with lethargy, poor contact, and poor feeding in early infancy;

Responds to combined treatment with biotin and thiamine

Leigh encephalomyelopathy

Thiamine and related vitamins may improve the outcome

Three distinct syndromes:

- A chronic peripheral neuritis, beriberi, which may or may not be associated with heart failure and edema;
- Acute pernicious (fulminating) beriberi (shoshin beriberi), in which heart failure and metabolic abnormalities predominate, without peripheral neuritis; and
- Wernicke encephalopathy with Korsakoff psychosis, which is associated especially with alcohol and narcotic abuse

Clinical Features of Thiamine Deficiency in Infants:

- **Early Symptoms:** Fatigue, apathy, irritability, poor concentration, anorexia, nausea, abdominal discomfort.

- **Neurological Symptoms:** Peripheral neuritis, decreased reflexes, loss of vibration sense, muscle cramps, ataxia, loss of coordination.
- **Cardiac Symptoms:** Dyspnea, tachycardia, cardiomegaly, ECG changes (QT prolongation, inverted T waves).
- **Ocular Symptoms:** Ptosis, optic nerve atrophy, ophthalmoplegia, nystagmus.
- **Other Symptoms:** Lactic acidosis, seizures, developmental delay in infants.

1. **CVS/Neurological Symptoms:**
    - **Beriberi:** A classic manifestation, with two forms:
        - **Wet Beriberi:** Cardiovascular symptoms like tachycardia, cardiomegaly, and high-output heart failure.
        - **Dry Beriberi:** Neurological symptoms including peripheral neuropathy, muscle weakness, and pain.
    - **Infantile Beriberi:** Occurs in exclusively breastfed infants of thiamine-deficient mothers, presenting with:
        - Crying, irritability, and sleep disturbances.
        - Progressive neurological signs like convulsions and encephalopathy.
        - In severe cases, cardiac involvement leading to heart failure.

Aspect	Dry Beriberi	Wet Beriberi
Primary Involvement	Neurological system	Cardiovascular system
Symptoms	- Peripheral neuropathy (tingling, numbness in limbs)	- Shortness of breath, especially during physical activity

	- Muscle weakness and pain	- Swelling of the lower legs (edema)
	- Difficulty walking	- Elevated heart rate (tachycardia)
	- Paralysis in severe cases	- Enlarged heart (cardiomegaly)
Physical Signs	- Loss of reflexes	- Congestive heart failure symptoms
	- Muscle atrophy	- Jugular venous distension
	- Decreased muscle tone	- Lung congestion
Onset	Gradual	Can be acute or gradual
Pathophysiology	Damage to peripheral nerves due to thiamine deficiency	Impaired cardiac function due to thiamine deficiency
Risk Factors	Chronic alcoholism, malnutrition, certain chronic diseases	Malnutrition, chronic alcoholism, high carbohydrate diet
Treatment Response	Rapid improvement with thiamine supplementation	Rapid symptomatic relief with thiamine, diuretics may be required for edema
Prognosis	Good with early treatment; can lead to irreversible damage if untreated	Can lead to life-threatening heart failure if untreated

2. **Gastrointestinal Symptoms:**
    - Anorexia and weight loss.
    - Constipation or diarrhea.
    - Abdominal discomfort.
3. **Developmental Delays:**
    - Poor growth and weight gain.
    - Delay in developmental milestones.
4. **Cardiovascular Symptoms:**
    - Tachycardia and enlarged heart.
    - Signs of congestive heart failure in severe cases.
5. **Muscular Symptoms:**

- Muscle wasting and weakness.
- Decreased muscle tone.

6. **Ophthalmological Signs:**
    - Nystagmus (involuntary eye movement).
    - Strabismus (crossed eyes).
7. **Other Symptoms:**
    - Lactic acidosis in severe cases.
    - Susceptibility to infections due to impaired immune response.

Diagnosis and Management:

- **Diagnosis:**
    - Based on clinical presentation, dietary history, and response to thiamine supplementation.
    - Laboratory tests may include blood thiamine levels, though not routinely done.
- **Management:**
    - Immediate thiamine supplementation, often resulting in rapid clinical improvement. This is usually done parenterally with 10-25 mg of thiamine intramuscularly or intravenously, followed by 5-10 mg per day orally.
    - Addressing nutritional deficiencies and ensuring a balanced diet.
    - Monitoring for cardiac and neurological recovery.
    - Education of caregivers about dietary sources of thiamine.

Prevention:

- Ensuring adequate thiamine intake in pregnant and breastfeeding women.
- Diversification of infant diet with thiamine-rich foods when appropriate.
- Supplementation in populations at risk of thiamine deficiency.

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8.a. Alkaptonuria

- Alkaptonuria, with a prevalence of approximately 1 in 200,000, represents a rare autosomal recessive disorder characterized by a disruption in tyrosine catabolism
- This disruption is due to a deficiency in the enzyme homogentisate 1,2-dioxygenase (also known as homogentisic acid oxidase), leading to the accumulation and subsequent excretion of large quantities of homogentisic acid (HGA) in the urine
- The pathophysiological hallmark of alkaptonuria is the deposition of oxidized HGA pigment in connective tissues, a phenomenon termed ochronosis
- Alkaptonuria exemplifies a classic inborn error of metabolism with a distinct biochemical basis and clinical presentation
- Its management is currently supportive and symptomatic, with ongoing research into more definitive treatments
- As a geneticist, understanding the molecular underpinnings of alkaptonuria is crucial for accurate diagnosis, patient counseling, and the exploration of novel therapeutic avenues.

Pathophysiology and Biochemical Mechanism

- **Enzymatic Deficiency**: The deficiency of homogentisate 1,2-dioxygenase in the tyrosine degradation pathway leads to the accumulation of HGA.
- **Ochronosis**: Polymerization and deposition of oxidized HGA in connective tissues cause ochronosis, manifesting as pigmentation and degenerative changes.

Clinical Manifestations

- **Dark Urine**: A characteristic feature, often noticeable in infancy. The urine turns black upon exposure to air due to the oxidation of HGA.
- **Late Onset Symptoms**: Although alkaptonuria may be asymptomatic in early life, symptoms typically emerge in middle age.
- **Scleral Pigmentation**: Gray-brown pigmentation of the sclera often appears after age 30.
- **Ear Pigmentation**: Darkening of the concha, anthelix, and helix of the ear, usually developing post-30 years of age.

- **Ochronotic Arthritis**: Presents with pain, stiffness, and limited motion in large joints like hips, knees, and shoulders, often mistaken for rheumatoid arthritis.
- **Cardiovascular Involvement**: Increased risk of degenerative heart disease in older patients, with pigmentation of heart valves.
- **Renal and Prostatic Calculi**: Occasional development of pigmented calculi.
- **Skin Pigmentation**: Occurs in some patients.

Diagnosis

- **Urine Analysis**: Suspected in patients whose urine darkens to black. HGA in urine can be identified by organic acid analysis or specific colorimetric tests.
- **Genetic Testing**: Confirmation of the diagnosis through genetic testing for mutations in the HGD gene.

Treatment and Management

- **Symptomatic Treatment**: Management of ochronotic arthritis and other symptoms is largely symptomatic.
- **Nitisinone**: This drug, used in tyrosinemia type I, reduces urinary excretion of HGA. Its long-term efficacy in preventing alkaptonuria complications is under investigation.
- **Lifestyle Modifications**: Including exercise and weight management to alleviate joint symptoms.
- **Monitoring**: Regular monitoring for the development of complications, particularly in the cardiovascular system.

Research and Future Directions

- **Preventive Strategies**: Research is ongoing to determine if early intervention can prevent the degenerative changes associated with ochronosis.
- **Gene Therapy**: As a genetic disorder, gene therapy may offer potential future treatment options.

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8.b. JMML

- Juvenile Myelomonocytic Leukemia (JMML) is a rare and aggressive hematopoietic malignancy of early childhood, characterized by the overproduction of myelomonocytic cells.
- It falls under the category of myelodysplastic/myeloproliferative diseases and represents a unique clinical and biological entity with distinct pathophysiological mechanisms.
- JMML represents a challenging pediatric oncology entity due to its aggressive nature, complex pathophysiology, and limited treatment options.
- The management of JMML requires a multidisciplinary approach, encompassing accurate diagnosis, risk stratification, and an individualized treatment plan.
- Advances in our understanding of the molecular genetics of JMML are paving the way for novel therapeutic strategies, which are critically needed to improve outcomes for affected children.

Pathophysiology and Molecular Genetics

- **Clonal Hematopoietic Disorder**: JMML is a clonal disorder of hematopoietic progenitor cells. It exhibits both myelodysplastic and myeloproliferative features.
- **Genetic Abnormalities**: The disease is associated with various genetic abnormalities, including mutations in the RAS pathway (e.g., NF1, KRAS, NRAS), PTPN11, and CBL genes. These mutations lead to constitutive activation of the RAS-MAPK signaling pathway, driving uncontrolled cell proliferation.
- **Epigenetic Dysregulation**: Recent studies suggest a role for epigenetic dysregulation in JMML pathogenesis, although this area requires further exploration.

Clinical Presentation

- **Age of Onset**: Typically affects children under the age of four.
- **Symptoms**: Include fever, pallor, skin rash, hepatosplenomegaly, lymphadenopathy, and a propensity to develop infections.

- **Hematological Findings**: Characterized by leukocytosis with monocytosis, anemia, and thrombocytopenia. Bone marrow examination typically reveals hypercellularity with increased myelomonocytic cells.

Diagnostic Criteria

- **WHO Guidelines**: Diagnosis is based on clinical features, peripheral blood and bone marrow findings, and genetic studies.
- **Exclusion of Other Disorders**: Important to differentiate JMML from other childhood leukemias and myeloproliferative disorders.

Treatment and Prognosis

- **Chemotherapy**: Conventional chemotherapy has limited efficacy and is primarily used to stabilize the disease or as a bridge to more definitive treatment.
- **Hematopoietic Stem Cell Transplantation (HSCT)**: Currently, the only curative treatment for JMML. However, the relapse rate post-transplantation remains significant.
- **Targeted Therapies**: Emerging research on targeted therapies, particularly inhibitors of the RAS pathway, offers potential new treatment avenues.
- **Prognostic Factors**: Factors such as age at diagnosis, platelet count, and specific genetic mutations can influence prognosis.

Drug/Therapy	Mechanism of Action	Role in JMML Treatment
Cytarabine (Ara-C)	Antimetabolite that interferes with DNA synthesis	Used in chemotherapy regimens, often as a bridge to hematopoietic stem cell transplantation (HSCT)
6-Mercaptopurine (6-MP)	Purine analog that inhibits DNA and RNA synthesis	May be used in combination with other chemotherapeutic agents for disease stabilization
Azacitidine	DNA methyltransferase inhibitor, induces hypomethylation of DNA	Investigated for its potential to modify disease course by targeting epigenetic dysregulation

Hydroxyurea	Inhibits ribonucleotide reductase, reducing DNA synthesis	Used for cytoreduction and control of leukocytosis
Interferon-alpha	Immunomodulatory agent	Has shown some efficacy in controlling symptoms and reducing spleen size
Ruxolitinib	JAK1/2 inhibitor	Being explored for its role in targeting aberrant JAK-STAT signaling in JMML
Sorafenib	Kinase inhibitor targeting RAF/MEK/ERK pathway	Investigational use in cases with specific mutations in the RAS pathway
Hematopoietic Stem Cell Transplantation (HSCT)	Replacement of the diseased marrow with healthy donor stem cells	Currently the only curative treatment option for JMML

- **Supportive Care**: In addition to these therapies, supportive care (e.g., management of infections, transfusions) is a critical component of JMML treatment.

Research and Future Directions

- **Molecularly Targeted Therapy**: Ongoing research is focused on developing targeted therapies that inhibit the aberrant signaling pathways in JMML.
- **Genomic Studies**: Comprehensive genomic studies are crucial for understanding the disease's heterogeneity and for the development of personalized medicine approaches.
- **Improving HSCT Outcomes**: Research is ongoing to improve the outcomes of HSCT, including reducing the risk of relapse and managing graft-versus-host disease.

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9.a. ADEM

- Acute Disseminated Encephalomyelitis (ADEM) is a demyelinating disorder of the central nervous system, predominantly affecting children and characterized by a widespread, often abrupt, inflammatory response following infection or vaccination.

- ADEM represents a severe, immune-mediated response to external stimuli, such as infections or vaccinations, leading to widespread demyelination in the CNS.
- Its acute management involves high-dose glucocorticoids, with plasma exchange or IVIG as second-line therapies.
- The prognosis is variable and largely dependent on the severity of the initial presentation.
- Distinguishing ADEM from MS, particularly in adults, requires careful clinical and radiological assessment.
- The reduction in ADEM incidence due to the use of modern vaccines underscores the importance of continued advancements in vaccine technology.

Epidemiology

- **Incidence**: ADEM is more common in children, with postinfectious encephalomyelitis frequently following childhood viral exanthems.
- The incidence following measles is about 1 in 1000 cases, and for varicella, it is between 1 in 4000 to 10,000 cases.

Pathophysiology and Etiology

- **Cross-Reactive Immune Response**: ADEM is hypothesized to result from an autoimmune response where the immune system, triggered by an infection or vaccine, mistakenly attacks myelin in the CNS.
- **Infections and Vaccinations**: Commonly associated with viral exanthems (measles, varicella, rubella, mumps, influenza, Epstein-Barr, HIV), Mycoplasma infections, and certain vaccinations (smallpox, Semple rabies, Japanese encephalitis vaccines).
- **Autoantibodies**: Autoantibodies to myelin basic protein (MBP) and other myelin antigens have been detected in CSF of ADEM patients, although direct viral invasion of the CNS is typically not observed.

Clinical Manifestations

- **Onset and Progression**: Rapid onset, often within hours to days post-infection or vaccination. In postinfectious ADEM, symptoms typically begin as the primary infection is resolving.

- **Neurological Symptoms**: Include fever, headache, meningismus, lethargy, coma, seizures, hemiparesis or quadriparesis, sensory loss, and brainstem involvement. Cerebellar involvement is notable in varicella-associated ADEM.
- **CSF Analysis**: Shows modest protein elevation, lymphocytic pleocytosis, and occasionally transient oligoclonal bands.

Diagnostic Considerations

- **History and MRI Findings**: Diagnosis is supported by a history of recent infection or vaccination and characteristic MRI findings (extensive white matter hyperintensities on T2/FLAIR sequences, gadolinium enhancement).
- **Differential Diagnosis**: Includes herpes simplex encephalitis, HIV, hypercoagulable states, vasculitis, neurosarcoidosis, metastatic cancer, and multiple sclerosis (MS). Distinguishing ADEM from MS can be challenging, especially in adults.

Treatment and Prognosis

- **Glucocorticoids**: High-dose glucocorticoids – Methylprednisolone, are the initial treatment, similar to management strategies for neuromyelitis optica (NMO).
- **Plasma Exchange or IVIG**: Considered in patients who do not respond to steroids.
- **Prognosis**: Varies with the severity of the acute illness. Measles encephalomyelitis, for instance, has a higher mortality rate and risk of permanent neurological sequelae.

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9.b. Diagnosis and treatment of steroid resistant nephrotic syndrome

- **Definition:** Steroid-Resistant Nephrotic Syndrome (SRNS) is characterized by the absence of remission despite four weeks of daily prednisolone therapy.
- **Initial Approach**:
    - Begin with genetic testing in specific cases and a kidney biopsy unless certain conditions are met.

- For monogenic SRNS, consider genetic counseling, ACE inhibitors, ARBs, and supportive management.
- In non-genetic SRNS where genetic testing is not indicated, commence with Calcineurin Inhibitors (CNI) and tapering steroids, along with ACE inhibitors/ARBs and supportive management.

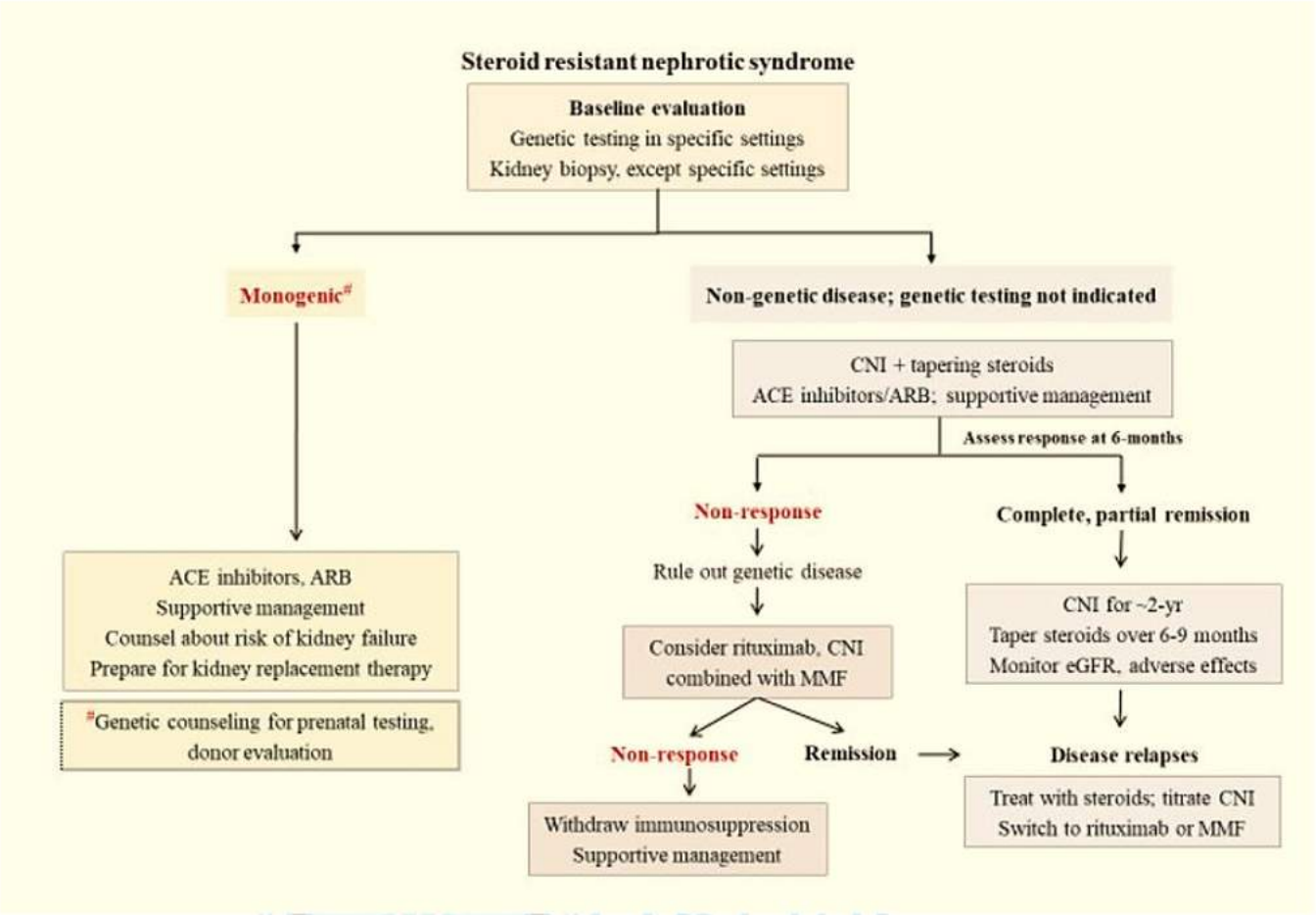
- **Assessment of Therapy**:
  - Evaluate response at 6 months.
  - If there's no response, rule out genetic disease, and consider adding rituximab, CNI combined with MMF (mycophenolate mofetil).
  - In cases of remission, continue CNI for approximately 2 years, taper steroids over 6-9 months, and monitor eGFR and for adverse effects.
  - In the case of relapse, treat with steroids, titrate CNI, or switch to rituximab or MMF.
- **Medication Dosing and Monitoring**:
  - **Tacrolimus**: 0.1-0.2 mg/kg/day in 2 divided doses; max initial dose 4 mg/day. Monitor blood levels.
  - **Cyclosporine**: 3-5 mg/kg/day in 2 divided doses; max initial dose 200 mg/day. Monitor blood levels.
  - **Prednisolone on alternate days**: 1.5 mg/kg for 4 weeks, then taper to 0.3-0.5 mg/kg for ~6-9 months.
  - **Cyclophosphamide**: 500-750 mg/m² IV every month for 6 months.
  - **Rituximab**: 375 mg/m² every 2 weeks for 2-4 doses.
  - **Mycophenolate mofetil**: 600-1200 mg/m² in divided doses.
- **Adverse Effects and Their Monitoring**:
  - Tacrolimus and Cyclosporine can cause nephrotoxicity and other systemic effects, requiring regular monitoring of renal function, blood pressure, and other parameters.
  - Prednisolone can cause weight gain, hypertension, and glucose intolerance, among other side effects.
  - Cyclophosphamide's adverse effects include leukopenia and hemorrhagic cystitis.
  - Rituximab has risks such as infusion reactions and infections.

- Mycophenolate mofetil may lead to leukopenia, liver dysfunction, and gastrointestinal issues.

- **Monitoring Regimens**:
  - Screen for cosmetic side effects, tremors, diarrhea, and hypertension.
  - Regularly assess blood glucose, liver function tests, and blood counts.
  - Evaluate for opportunistic infections and check immunoglobulin levels with drugs like rituximab.

- **Further Considerations**:
  - In case of non-response to initial treatments, withdrawal of immunosuppression and supportive management is advised.
  - Continuous re-evaluation of therapy effectiveness and side effects is critical for managing SRNS effectively.
  - Disease relapse requires a return to aggressive treatment or an alteration in the therapeutic regimen.

The management of SRNS must be personalized, taking into consideration the patient's response to treatment, the side effects experienced, and any underlying genetic conditions.



Specific advances:

Genetic Insights and Molecular Diagnostics

- **Genetic Testing**: Identification of mutations in genes like NPHS1 (nephrin), NPHS2 (podocin), WT1, and others.
- **Personalized Medicine**: Tailoring treatment based on genetic findings, especially in congenital and infantile forms of SRNS.

Immunosuppressive Therapies

- **Calcineurin Inhibitors**: Cyclosporine and tacrolimus remain mainstays for SRNS, aiming to induce remission.
- **Mycophenolate Mofetil (MMF)**: Used as a steroid-sparing agent or in calcineurin inhibitor-intolerant patients.
- **Rituximab**: An anti-CD20 monoclonal antibody, showing promise in certain SRNS cases, especially those with frequent relapses or calcineurin inhibitor dependence.

Novel Therapeutic Agents

- **Acthar Gel (ACTH)**: Demonstrated efficacy in inducing remission in some SRNS cases.

- **Abatacept**: A CTLA-4-Ig fusion protein, showing potential in B7-1 mediated SRNS.
- **Belimumab**: A B-lymphocyte stimulator-specific inhibitor, currently under investigation.

Emerging Research and Trials

- **Stem Cell Therapy**: Investigating the role of stem cells in renal repair and regeneration.
- **Gene Therapy**: Potential future approach for genetically driven forms of SRNS.
- **Biomarkers**: Research into urinary and serum biomarkers for early detection and monitoring of disease progression.

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10.a. Enumerate causes of AFP

List of extended causes of AFP that are important to include in surveillance:

1. ***Guillain-Barré Syndrome (GBS)***: An autoimmune disorder causing muscle weakness and paralysis.
2. ***Transverse Myelitis***: Inflammation of the spinal cord leading to neurological deficits.
3. ***Enteroviral Infections Other Than Polio***: Such as enterovirus 71, associated with hand, foot, and mouth disease.
4. ***Traumatic Neuritis***: Nerve damage due to injury.
5. ***Hypokalemic Paralysis***: Caused by a sudden drop in potassium levels.
6. ***Tick Paralysis***: Resulting from neurotoxins released by tick bites.
7. ***Rabies (Post-rabies Vaccine Neuralgia)***: Rarely, paralysis can occur after rabies or its vaccine.
8. ***Peripheral Neuropathy***: Including hereditary and acquired neuropathies.
9. ***Myasthenia Gravis***: An autoimmune disorder affecting neuromuscular junctions.
10. ***Spinal Muscular Atrophy***: A genetic disorder affecting motor neurons in the spinal cord.
11. ***Botulism***: Caused by toxins from Clostridium botulinum.

12. ***Acute Toxic Neuropathies***: Such as from heavy metal poisoning.
13. ***Infectious Myelitis***: Including viral, bacterial, parasitic, and fungal infections.
14. ***Post-Infectious Encephalomyelitis***: Following viral or bacterial infections.
15. ***Neurological Complications of Systemic Illnesses***: Such as lupus, sarcoidosis.
16. ***Vaccine-Associated Paralytic Poliomyelitis (VAPP)***: Rarely associated with the oral polio vaccine.
17. ***Congenital Myopathies and Muscular Dystrophies***: Presenting early in life with muscle weakness.
18. ***Spinal Cord Compression***: Due to tumors, abscesses, or herniated discs.
19. ***Metabolic Disorders***: Such as hypoglycemia or hyperglycemia causing muscle weakness.
20. ***Critical Illness Polyneuropathy and Myopathy***: In patients with severe systemic illness.

Importance in Surveillance:

- ***Differential Diagnosis***: Helps in distinguishing polio from other causes of AFP.
- ***Public Health Management***: Assists in identifying and managing outbreaks of non-polio AFP.
- ***Resource Allocation***: Guides healthcare resources to appropriate areas.
- ***Epidemiological Tracking***: Monitors trends and patterns in AFP causes.

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10.b. Define migraine and classify

Definition of Migraine in Children

- Migraine in children is a recurrent headache syndrome characterized by pulsatile headaches often accompanied by symptoms such as photophobia, phonophobia, nausea, and/or vomiting.
- It is the most common acute and recurrent headache disorder in this age group.

Classification of Migraine in Children

Migraine without Aura

- **Clinical Features**: Moderate to severe headache, usually unilateral, pulsating quality, aggravated by physical activity.
- **Diagnosis**: Clinical, supported by imaging if needed.